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Original Articles for August, 1959

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Clinical Medicine

Vol. VI, No. 8

CONTENTS FOR AUGUST, 1959

Guest Editorial

Original Articles

...threatened abortion

...habitual abortion

...endometriosis

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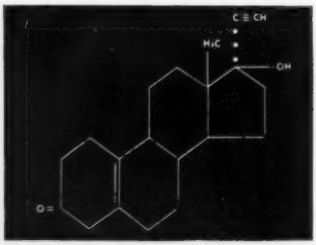

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Research in the Service of Medicine.

1. Symposium on New Steroid Compounds with Progestational Activity, Ann. New York Acad. Sc. 71:483-805 (July 30) 1958.
2. Edgren, R. A.: The Uterine Growth-Stimulating Activities of 17α-Ethynyl-17-Hydroxy-5(10)-Estren-3-One (Norethynodrel) and 17α-Ethynyl-19-Nortestosterone, Endocrinology 62:689 (May) 1958. 3. Rakoff, A. E.: Pages 800-805 of reference 1.
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GUEST EDITORIAL

Health For Peace

Working together to conquer suffering and disease may promote understanding between nations

JAMES E. M. THOMSON, M.D., *Lincoln, Nebraska*

The quest of Peace after two World Wars seems to be doomed by circumstances beyond the control of diplomatic and political ideologies with their multipurpose interests and a mutual distrust. Recognition of the technical advances of the Twentieth Century in the form of speeded-up communications, transportation, industry, commerce and above all the possibilities of human annihilation by total destruction have shrunk the world's size to the extent that we have become merely a world community of individual neighborhoods—some industrial, commercial, and residential, and some shamefully neglected slums. The basic issue challenging these neighborhoods may be summarized in two words: Peaceful Coexistence.

WE ARE ALL INTERDEPENDENT, NOT INDEPENDENT

Most nations in this world community realize that, for self preservation, *inter*dependence is essential in this closely united mixed society comprising every color, race, religion and ideology. Every nation must adhere to the tenet of appreciation for problems of security, economy, racial and general welfare of their neighbors for abiding peace. To put this into the simple words of our Christian teachings we are "our brother's keeper."

Some years ago, Arnold Toynbee, writing in the New York Times Sun-

day Magazine Section, stated "the bered . . . as an age in which human 20th Century will be chiefly remem- society dared to think of the welfare of the whole human race as a practical objective." Most efforts in this direction have been, since World War II, under the auspices of local governments, religious organizations, World Health Organization, United Nations and many private foundations, in cooperation with men of medicine, science, and in the realm of technical health assistance, endeavoring to bring a better way of life to the peoples of war-ravaged and under-privileged sections of the globe. The U.N., in recognition of this multilateral responsibility, has established special agencies to render such technical assistance. This type of international diplomacy has lead to a better understanding among these peoples of our unselfish generosity and of our down-to-earth approach to the problems of health, rehabilitation and general welfare. The impact of this has proved an inspiration to the medical professions of these countries and has given encouragement to the many sick and disabled.

THE RIGHT KINDS OF FOREIGN AID

It is a type of foreign aid that the needy can sense, and appreciate far more than great road projects, power plants or military installations. There is something of a homey quality and humane approach in this exchange of medical techniques, scientific research and therapeutic discoveries, that leads to a mutual respect and bond of union that is impossible to attain by any other means.

No matter what the political policies or economic attitudes of the country may be, no one can question the integrity, purpose or unselfishness of giving or exchanging information pertaining to better health and better living, as these are essential to peaceful progress in human happiness. Howard Rusk has so aptly said: "Health including rehabilitation services for the handicapped is fundamental to the prime democratic concept of equal opportunity for all. A world in which good health is enjoyed by but a few cannot be a politically stable world." How can a man in pain, disability, dire poverty and distress fight for the principles of democracy and freedom? Unless he can work and produce, how can he supply his most elemental needs, and become a customer for the goods which all the world wants to sell him?

"EVERY MAN A KING"

The surge of nationalism and self-determination has seized the under-privileged sections of the globe with fanatical tenacity. The setting up of independent nations has been encouraged in areas with little civilization, where poverty and disease are rampant. If they are to succeed and take a useful place in the world society, we must assume a greater responsibility for their healthful existence as well as social and intellectual improvement. During my visits in recent years to some of these areas, it was not difficult to imagine how precarious their future is on seeing the extent of poverty in everything that makes life even tolerable to us. The opportunity for health is essential to the realization of self-sufficiency. Dr. Charles Mayo sums it up simply by—"1. Sickness makes people poor. 2. Poverty makes people sick." Health makes for ambition, productiveness, happiness and peacefulness. Without health and vital capacity military supplies are of

no value. Unless healthy, a nation cannot be expected to be wealthy and wise. By our sharing our medical science, educational and research resources with these underprivileged neighbor countries, we are pointing the way to developing their economic resources, productive capacity and better living conditions, through a more healthful existence. Further we bring prestige for our principles and ideals and demonstrate to the world the unselfishness of western peoples, without dictating their policies, politics and beliefs.

DOES HEALTHFULNESS MAKE FOR PEACEABLENESS?

A healthful world is a peaceful world and within the last year, Executive and Legislative branches of our government have recognized the importance of the International Health for Peace movement by declaration, and legislation enacted or pending. A year ago last January, in his State of the Union message, President Eisenhower proposed a "Science for Peace" plan to "obtain a good life for all." As a first step, he invited the Soviet Union to join in the current five-year program of the global eradication of malaria and expressed a willingness to pool our efforts with those of Russia and other countries against cancer and heart disease. "If people can get together on such projects," he asks, "is it not possible that we can then go on a full schedule cooperative program of science for peace."

Senator Humphrey reported that, during the first two hours of his visit with Soviet Premier Nikita Khruschev, the premier expressed enthusiastic approval of such a proposal. To quote the Senator, "during my interview with the Premier, I had noted that areas of disagreement between our respective foreign policies remained broad and deep. It does not appear that for a considerable time these differences will be resolved. In the meantime, we need to learn how to work together and the best place to start is in a non-political area. The world is hungry for some evidence of effective Soviet-American collaboration. One of the best areas in which to start is in the field of health . . .". "The time to act on Health for Peace is now. Human beings are dying in vast numbers in Africa and South Asia from malaria and tuberculosis; from other infectious diseases in the United States, the USSR, Latin-America, Europe and Australia. Politicians may continue to wrangle, but doctors, nurses, midwives and others, can now cure and heal and relieve suffering and it is the latter goal that mankind desires."

"Mankind has heard enough and seen enough of the atom and hydrogen bombs, now let mankind see and hear more of the only kind of destruction we want; the elimination of man's ancient enemy, disease."

The strong support to the imaginative and sound proposal of President Eisenhower of Science for Peace has led to the introduction of a bill by Senator Lester Hill, with the co-sponsorship of many other senators, for the creation of a National-International Medical Research Project within the National Institutes of Health, to encourage and support research, exchange information on research, to train research personnel and improve research facilities throughout the world. This bill, called the "Health for Peace" bill, has stimulated nationwide interest. A large citizens' committee has been formed to increase

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public understanding of the principles underlying the importance of the United States support of international health work. The moving spirits of this committee are General Omar Bradley, chairman; and Howard Rusk, executive vice chairman. Dr. Rusk has given generously of his time to this cause, both in his writings and addresses before influential groups.

Passage of this bill in no-wise interferes with other programs of an international health nature, but merely augments them with the increased purpose of training for and stimulating these needy nations in health programs and research.

CONCLUSION

We United States doctors should lend our influence and make our personal contribution to such much needed health programs for suffering humanity in our world community of negihborhood nations. Working in harmony toward victory over disease where ever it exists, brings us closer together for health, happiness and human understanding in our struggle for peace.

A British philosopher of 400 years ago said all this so simply in one sentence, "If every man would mend a man, then would all the world be mended." ◄

Cancer of the Paranasal Sinuses

If a patient is consistent in relating bizarre complaints to one or the other side, the otolaryngologist should be alerted to the possibility of cancer in or around the paranasal sinuses. Diagnosis can be made by thorough anterior and posterior rhinoscopy and biopsy. Usually more difficult technics must be employed—as antral washings with Papanicolaou stains, sinus x-rays with basal and lateral views and/or radiopaque study with water-soluble contrast media.

Total maxillectomy, alone or combined with an exenteration of the orbit, is advocated when the lesion is believed to be local, of 2 to 2½ cm., and in a surgically favorable location. Most favorable sites are the medial and anterior walls of the antrum. If disease remains, radium is inserted postoperatively. In some selected very early cases resection of the maxilla is done.

The maximum surgical attempt is advocated when the pterygoids are involved if the patient can adapt to disfigurement and interruption of function. Usually this means exenteration of the orbit.

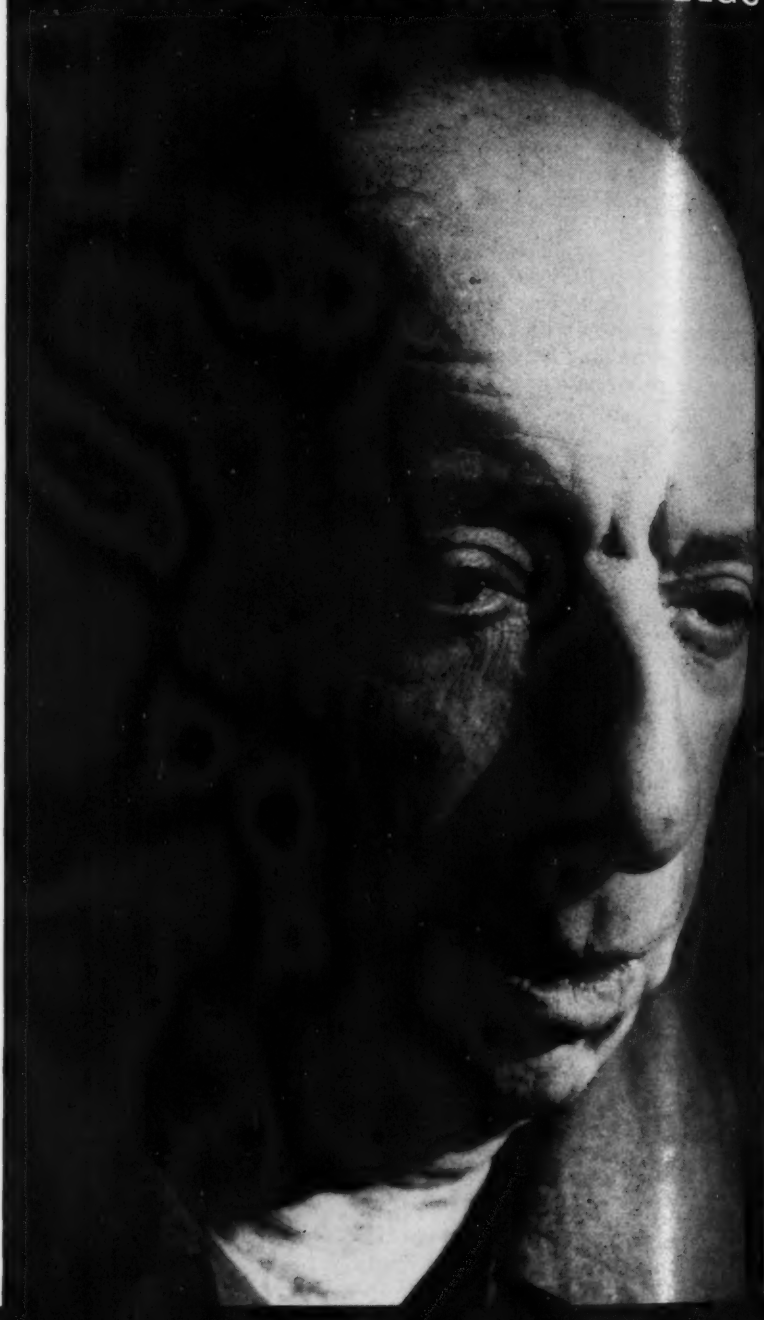
Local recurrences at the operative site are treated by x-rays using the cone to concentrate the rays.

A plea is made for a high index of suspicion of neoplasm of the sinuses and for exploratory surgery in suspicious cases.

The patient should have the combined efforts of the radiologist and the surgeon. The patient who has added years of life, but who is in constant pain, unable to speak intelligibly, and unable to swallow, is a failure. Only a few cases of sinus carcinoma can be cured.

Sisson, G. A., & Johnson, N. E., *New York J. Med.*, 59:609-614,1959.

IN NAUSEA/VOMITING/VERTIGO



ORIGINAL ARTICLE

Physical Medicine in Treatment and Rehabilitation of Arthritis

Judicious application of heat, massage and exercise are therapeutic requirements in this disease

GEORGE TWOMBLY, JR., M.D., *Denver, Colorado*

Proper use of physical agents is an important feature of therapy of the patient with a chronic joint disease. The techniques can be applied and utilized with much success by the general practitioner who is interested and reasonably well informed in this field. If the arthritic patient is to receive maximum benefits from his physical treatment, the physician must be able to not only prescribe the initial therapy, but to supervise its administration and the response, change the therapy as needed, and periodically recheck the physical treatment program. The doctor who cannot provide such a service for his arthritic patient should solicit the services of a colleague who is able to do so.

The final decision in this as in all medical matters must be made by the physician. Haphazard use of physical agents should be discouraged. A definite diagnosis confirmed by x-ray and laboratory studies as needed should be made before prescribing physical treatment. Such conditions as rheumatic fever, collagen diseases, gout, pyogenic or tuberculous joint involvement must be distinguished from chronic arthritis. If the decision is made to employ physical treatment for symptomatic relief during the early stages while diagnostic studies are

being made, the regimen should be conservative.

The main objectives are to relieve pain, increase and maintain range of motion of the involved joints, relieve secondary fibrositis and myositis, and improve function and independence.

Most patients with either osteoarthritis or rheumatoid arthritis should have at least a trial of physical therapy in addition to their other treatment. Partial temporary relief of pain with drugs enables the patient to better participate in the physical treatment program.

HEAT

Heat is indicated to improve local circulation, relieve pain and as a preliminary to massage and exercise. It is essential that selection be made of the proper source of heat and the optimum intensity, duration and frequency of its use. In the early acute febrile stage of rheumatoid arthritis the application of generalized or even local heat to the joints may not be indicated. A less vigorous and intense utilization of heat and exercise is usually more beneficial and better tolerated during the acute phase of arthritis. A deeper, more penetrating type of heat—such as diathermy or ultrasound can usually be much better tolerated and provide better therapeutic results when applied during the chronic stages. The mildest form of heat that can be tolerated and yet achieve therapeutic results should be selected.

Before prescribing any form of heat, the patient should be questioned about previous use of heat and the response. Many arthritic patients can relate whether they have reacted better to moist or dry heat and this will assist the physician in his initial heat prescription. Mild, superficial forms of heat—such as infra red, hot packs, heating pads, hydrotherapy — will often suffice. Other common and acceptable forms are short-wave diathermy, ultrasound, moisture cabinet, paraffin bath and contrast baths. Caution should be used in treating elderly persons with cardiovascular disease by generalized heat, and in using local heat on patients with peripheral vascular disease.

MASSAGE

Massage can provide a sedative effect in relieving pain and spasm. For best results, massage is usually preceded by some form of heat. Massage should not be administered directly over the involved joints, but only to the soft tissues proximal and distal to the joints. For those patients who have an associated secondary fibrositis, a fibrositic type of massage, in addition to appropriate heat, may be indicated.

EXERCISE

Exercise, carefully prescribed and properly used, can contribute more for the arthritic patient than any other form of physical treatment. The objectives are to increase or maintain range of motion of the joints, improve circulation, maintain and improve muscle tone, and strengthen and maintain functional efficiency. One should be specific in ordering the type, amount and technique of the exercise to be performed. It should be assumed that the patient does not understand the exercise regimen. Adequate supervised instruction should be given relative to technique and number of repetitions. There is a fine balance between over-exercise and under-exercise in either the acute or chronic case. Under exercise may contribute to partial or complete loss of motion; vigorous over-exercise may

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References: Batterman, R. C., et al.: New York J. Med. 58:3821, 1958. / Harrison, T. R.: Principles of Internal Medicine, 3rd ed. McGraw-Hill 1958, Pg. 1764. / DiMascio, A., et al.: Am. J. Psychiat., 115, 301-317, 1958. / Sainz, A.: Proc. of Mohawk Valley Psychiatric Assn., June 17, 1957. / Fleischmajer, R., et al.: Antib. Med. & Clin. Therap., 5, 120-124, 1958. / Hoekstra, J. B., et al.: J. Am. Pharm. A., 42, 587-593, 1953. / Cronk, G. H. and Naumann, D. E.: New York J. Med., 55, 1465-1467, 1955. Paper in preparation: data on 500 clinical cases available on request.

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result in irreparable joint damage. The patient should expect some slight increase in joint pain following his exercise sessions. If this persists for more than one day, the exercise is probably too intense, the repetitions too frequent, or the type incorrect.

For the patient with early joint involvement, proper employment of heat and exercise may help prevent contractures, muscle atrophy and joint restriction. For the more advanced case, exercises can assist in regaining some joint motion as well as maintaining muscle power.

A word or two should be said about the use of cervical traction. Many cases of cervical osteoarthritis, either with or without radiculitis, receive some relief of pain and increased range of motion from cervical traction. Such therapy should be applied under supervision at least during the first few applications, and then if it proves effective, the patient can continue with it at home.

The arthritic patient may have been seen by many physicians during the course of his disease, and various forms of physical therapy may have been used. It is important to have full information on this point. The physician should know what the patient expects of physical therapy. Some arthritics are overly optimistic, as to the potential benefits, seeking more than they should expect. Such overoptimism should be warned against. Others realize the chronicity of their condition and accept the prescribed physical medicine program as a useful adjunct in the total management of their disease. They are able to accept improvement rather than cure. Others are basically disgruntled, skeptical and pessimistic, accept each new therapeutic regimen with an attitude of frustration. They frequently feel they are wasting their time with a conservative type of treatment—such as, physical or occupational therapy—and thus their cooperation is poor.

Physical treatment in arthritis should always be administered with a long range view in mind. The patient should be informed early that he must assume an active role in the program. Except in the case of the severely involved acute rheumatoid arthritic who requires hospitalization, these patients should be instructed early and in great detail in a treatment program which can be followed at home. Periodic rechecks of the patient and his physical therapy program should be made by the physician in charge.

Physical medicine and rehabilitation techniques can play an important role in the treatment of arthritis. When properly utilized, both subjective relief and objective functional improvement are usually attainable goals.◄

ORIGINAL ARTICLE

Control of Hemorrhage During Pregnancy

The agent employed safely and effectively produces hemostasis without associated sympathomimetic activity

WILLIAM FITZGERALD, M.D., *Albany, New York*

Hemorrhage of non-endocrine origin occurring during pregnancy has both psychological and physiological effects, regardless of the site of the bleeding. Capillary bleeding may result from faulty coagulation of blood (hypoprothrombinemia), increased capillary permeability or fragility, and other causes which commonly accompany pregnancy. Following a severe hemorrhage, the two major changes in the blood picture are low blood count and low hemoglobin level. These changes, and the increased danger of inflammatory processes, make the patient a potentially poor obstetrical risk, unless specific corrective measures are employed immediately. The patient entering labor after a severe hemorrhage has been controlled will have a tendency to bleed more profusely than will a normal obstetrical patient.

FATAL SEPARATION OF FETUS

If more than 25 per cent of the placenta has become prematurely separated from the wall of the uterus, the fetus cannot be expected to survive. In one such case confirmed at the time of delivery by pelvic x-ray studies, bleeding was controlled and hemostasis established although the portions of the prematurely detached placenta which were found fibrosed at the time of delivery still had the same essential gross and microscopic structure of a normally implanted

placenta. Fortunately, in a certain percentage of these patients nature seals off the hemorrhagic area and allows the remaining portion of the placenta to provide the fetus with the oxygen and nutrition necessary for normal development. Thus, a fetus might survive even if 30 per cent of the placenta is detached from the uterine wall.

A POTENT HEMOSTATIC

This report describes the treatment of bleeding during pregnancy with carbazochrome salicylate*, a hemostatic agent without sympathomimetic activity[1-4] which effects hemostasis by increasing capillary resistance and promoting retraction of severed capillary ends. It reportedly influences the capillary intercellular cement substance so that the cells draw closer together and the ends of the capillaries constrict, causing a self-clamping mechanism similar to that by which the end of menstrual bleeding is brought about in the coiled arterioles left at the decidua basalis.[5]

The following two cases illustrate dramatic hemostatic responses achieved with carbazochrome salicylate.

CASE 1

A gravida III, para II, of 24 with three normal previous pregnancies. She was first seen in her fifth month, when she called to report a severe nosebleed. Blood pressure was 100/60; pulse rate 120. There was profuse bleeding from the right naris. A severe frontal headache with nausea and vomiting had preceded the nasal bleeding. One cc. carbazochrome salicylate was immediately administered intramuscularly. Within 20 minutes the bleeding diminished considerably, although the frontal headache persisted. The injection was repeated in 30 minutes and bleeding decreased further, blood pressure rose to 110/62, pulse rate to 100, apprehension was relieved, and bleeding diminished to a small drainage. The patient was closely observed and given 1 cc. carbazochrome salicylate twice daily intramuscularly for the next 72 hours, by which time all bleeding had disappeared, as had the headache and dyspnea. Once the hemorrhage was completely controlled, the patient was given capsules containing 65 mg. carbazochrome salicylate, 5 mg. vitamin K, 50 mg. hesperidin, and 100 mg. vitamin C, one three times daily for three weeks.* When no further bleeding had occurred, blood pressure was 118/68, pulse 80, respirations 20, and hemoglobin and hematocrit were restored to 12.5 level, RBC was 4,000,000 and WBC 9500.

An intramuscular injection of 1 cc. of an iron-dextran complex was given along with the first dose of carbazochrome salicylate and continued for five days in order to correct the moderate anemia resulting from the loss of blood. Oral ferrous gluconate was substituted for the parenteral iron after 5 days, and the patient was also given a high-protein, low-fat, low-salt diet to follow along with a multivitamin preparation. Her course during the remainder of the pregnancy was uneventful, and she bore a normal 6½ lb. child at full term without further bleeding. During the last three weeks of her pregnancy she was given three capsules of the hemostatic preparation daily to maintain normal blood coagulability and a normal prothrombin level, and to prevent any abnormal capillary permeability.

Postpartum convalescence was uneventful, and at the time of the mother's final examination the nasal cavity was clean without evidence of any opened blood vessels or areas of hemorrhage.

CASE 2

A gravida IX, para VI of 32 whose first pregnancy terminated at 4½ months in twin stillbirth. Succeeding pregnancies yielded four premature and two term deliveries. When first seen she was six- to eight-weeks pregnant, and normal except for hemoglobin 11.25 gm. Treatment was initiated with an antiabortifacient preparation containing ethisterone 15 mg., hesperidin complex

*Adrestat F®, Organon, Inc., Orange, New Jersey.

1. Roskam, J. and Derouaux, G., *Arch. Internat. Pharmacodyn.*, 69:348,1944.
2. Bacq, Z. M., *Compt. Rend. Soc. Biol.* 144:536,1957.
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175 mg., ascorbic acid 175 mg., sodium menadiol diphosphate 2 mg., and *dl* alpha tocopheral acetate 3.5 mg. per tablet,* the dosage being one tablet q.i.d She was also given 15 gr. ferrous gluconate daily, and a routine vitamin-diet-bedrest regimen. Two months later complaint was made of pain and moderate vaginal bleeding, for which she was hospitalized, and dosage of the antiabortifacient increased to two tablets four times daily.† Pain and bleeding subsided after 72 hours and the patient was discharged.

A month later she was again hospitalized with profuse vaginal bleeding and severe cramps, for which a regimen of morphine 1/6 gr. and bed rest was inaugurated. Bleeding diminished and she was discharged a week later, but was readmitted the following week with profuse bleeding and severe cramps, at which time carbazochrome salicylate was given intramuscularly four times daily until the bleeding was controlled. She was again discharged after one week, at which time x-rays revealed a separation of about 25 per cent of the placenta from the posterior wall of the uterus. Shortly thereafter she was hospitalized for recurrence of bleeding and given a daily injection of 1 cc. carbazochrome salicylate. When bleeding ceased within 10 days she was again discharged and placed on a regimen of modified bed rest at home along with one *Adrestat* capsule three times daily. No further bleeding episodes occurred, and at full term she delivered a 6¾ lb. boy which examination at 6 weeks showed to be healthy with no abnormality.

At delivery the area of the placenta where the hemorrhage had occurred was found sealed. There were areas of fibrinization and apparently not more than 25 per cent of the placenta was affected. The blood picture was normal at six weeks and at four months after delivery. As a precautionary measure one *Adrestat* capsule daily was administered for one month after delivery.

COMMENTS

To our knowledge Case 1 is the first report of a patient, five months pregnant, suffering severe nasal hemorrhage which was successfully controlled without complications. Similarly, Case 2 to our knowledge is the first report of fetal salvage with 25 per cent of the placenta detached.

DISCUSSION

The two cases described* illustrate the highly effective hemostatic activity of carbazochrome salicylate, an adrenochrome-semicarbazone-sodium salicylate complex which acts by constricting the severed terminals of small blood vessels. While the adrenochrome constituent of this complex is a derivative of adrenalin, and has an adrenalin-like effect on the terminals of the small vessels, unlike adrenalin it does not affect the cardiac rate or the blood pressure. Moreover, adrenalin in therapeutic doses must be used with extreme care and caution because of the danger of producing heart block and in certain patients symptoms of allergic shock, whereas carbazochrome salicylate initiates none of these untoward reactions.

All pregnant patients treated by the author receive bleeding- and clotting-time tests frequently in the last trimester and particularly in the last three weeks. Eighteen of these patients had demonstrated unduly prolonged clotting times and were placed on three of the hemostatic capsules daily for the remainder of their pregnancies. Within two weeks after the institution of this medication, clotting times were normal in every case, due apparently to the vitamin K and anticapillary fragility substances contained in the capsules. As a result of this finding the author now routinely prescribes *Adrestat* capsules, one three times daily to all pregnant

*Nugesterol, Organon, Inc., Orange, New Jersey.
†Although one must use hormone therapy judiciously, our experience with this preparation justified the increase dosage. We have followed 22 babies for a period of six months after delivery and observed no masculinization.

*These patients were delivered at the A. N. Brady Maternity Hospital, Department of O.B., Albany Medical College, Albany, New York.

patients during the last trimester of pregnancy.

SUMMARY

Hemorrhage during pregnancy may result in changes which make the patient a potentially poor obstetrical risk unless it is promptly controlled. An effective hemostatic for this purpose is carbazochrome salicylate, which in one presented case controlled nasal bleeding in a pregnant patient and in another uterine hemorrhage resulting from a prematurely separated placenta. No side effects were noted in these cases.

It is concluded from results obtained by the author that carbazochrome salicylate safely and effectively controls bleeding during pregnancy, particularly where the integrity of the smaller blood vessels has been affected. For this reason he employs it routinely in patients during their last trimester of pregnancy.◀

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ORIGINAL ARTICLE

Elimination of Pain in Office Procedures

A review of methods of preventing pain during the routine examination and treatment of patients is presented

PAUL WILLIAMSON, M.D., *Bellaire, Texas*

Unfortunately, we doctors are often needlessly careless in our offices about causing our patients pain. In many instances, the pain is avoidable. Here are a dozen examples of procedures which are more or less commonly done and about which patients complain bitterly.

EXAMINATION OF THE NOSE

The standard nasal speculum can be inserted and manipulated totally without discomfort. The sensitive membrane of the septum may be avoided if the speculum is inserted in a fashion that exerts pressure on the wing of the nose. It should be pointed slightly away from the tender septal area. The speculum should be inserted as though you were going to open the jaws vertically, and with a slight lateral pull. After the closed speculum has fallen in place, it may then be turned and opened at will. A 45° angle application is usually used, so that the handle points downward and slightly laterally. Two things are to be avoided: Putting too much pressure to bear and tickling the hairs in the end of the nose. You will save the patient a sneeze and yourself a good spraying by being careful not to touch them.

When working in the interior of the nose, for example in cannulizing the opening of the maxillary sinus, the area should always be thoroughly anesthetized. A 2 per cent solution of pontocaine with 2 per cent ephedrine

achieves shrinkage of the membrane as well as anesthesia. The solution is applied by means of cotton tampons inserted with the Wilde angular forceps. The original tampon should be left in place five minutes, then taken out and a new one inserted. The second one should also be left in place five minutes before any manipulation is attempted.

THE EYE: REMOVAL OF FOREIGN BODY

It is customary to anesthetize the eye for removal of a corneal foreign body, but it should be remembered that the conjunctiva is also sensitive. Unless any foreign body can be wiped away, you will save your patient pain and yourself trouble by instilling a local anesthetic into the eye before any manipulation. In using fluorescein dye to show up corneal abrasions or ulcers, it is good practice to anesthetize the eye before instilling the dye. This is not strictly necessary but will save your patient the sting of the fluorescein solution. Here, again, the common error is to instill the local anesthetic and to go to work immediately. Five to ten minutes are required to achieve complete local anesthesia.

THE THROAT

In any procedure that is likely to take more than a second or two, spray a solution of local anesthetic over the mucous membrane and let the patient wait five minutes before initiating the examination. An example of a painful procedure in the throat would be cauterization of small masses of lymphoid tissue or tonsillar tags. This, of course, can be done without anesthesia, but it just plain hurts. With the simplest of anesthetics, almost any procedure in the pharyngeal area can be rendered pain-free.

Again, the indication for this is more personal than medical. Sometimes it is these little things that count more than the procedure itself, at least in the mind of the patient.

THE EAR

The external otic canal is notoriously resistant to local anesthesia but should certainly be anesthetized for any sort of manipulation that would put pressure on the drum or that involves an inflamed area in the external canal. A solution of 1 or 2 per cent benzocaine in olive oil is satisfactory. General anesthesia is usually better for any technique that involves cutting the drum. Sometimes a whiff or two of trichloroethylene from an inhaler does the job nicely.

ABSCESS

The opening of a superficial abscess can be an extremely painful experience to the patient or it can be raised almost to the level of an art by the expert practitioner. The area over the abscess is cleaned gently and a small area to one side of the abscess is sprayed with ethyl chloride. Through this sprayed area a fine-gauged needle is inserted and a local anesthetic injected to provide a field block of the area surrounding the abscess. The patient is then asked to wait 10 to 15 minutes for the full effect of the anesthetic. Since pressure on the abscess will still cause pain, the skin on either side of the proposed incision is picked up with towel clips and pulled upward rather sharply during the time of the incision. A pointed knife blade is inserted into the abscess with a quick movement and jerked out with the cutting edge uppermost, laying the abscess wide open. Unless there is a definite reason to believe that the abscess is multilocular, it

should be left alone. Drainage is encouraged by means of hot packs without manipulation.

CYSTOSCOPY

This simple and good procedure is one that is frequently maligned since it is believed that cystoscopy is a very painful thing. Extremely careful manipulation of the cystoscope will allow examination of most of these patients without any discomfort at all. The practice of giving either morphine or a sedative before the procedure is not recommended. The cystoscope is lubricated with olive oil (sometimes a small amount of benzocaine is added to the oil) and is allowed to fall into the bladder under its own weight. Never more than the gentle pressure of one finger should be needed for the ordinary cystoscopy. In the event of spasm at the bladder neck which obstructs the free passage of the instrument, press gently on the scope until the pressure overcomes the muscle spasm.

With the instrument inserted in the bladder, extreme care should be used in its manipulation so that no pressure is used which might be painful to the patient. When proper care is used, only about one of every 20 patients will complain of any pain at all. In the examination of a hypersensitive individual who finds even the most minor procedure painful, it might to wise to instill a 1.5 per cent solution of metycaine into the urethra previous to and, occasionally, during the process. There have been no ill-effects reported from this.

SIGMOIDOSCOPY

This procedure also may be accomplished almost without pain. One of the more common errors is to forget the direction taken by the anal canal and by the rectum. The anal canal, an inch long, runs forward and upward. With the patient in jackknife position, the sigmoidoscope should be pointed at the navel and should be inserted with a minimum of pressure. There is only the force of the anal sphincter to be overcome, and this may be done by steady, gentle pressure. Once the scope is past the anal canal, its direction is changed so that it points straight upward toward the neck and it is advanced under direct vision, the gut being *gently* distended with air so that the operator sees the exact course to follow. Never use excessive pressure while working with the scope.

INTRAMUSCULAR AND INTRAVENOUS INJECTIONS

A major source of complaints is the administration of medicine IM and IV. The gluteal area is divided arbitrarily into quadrants, and the upper outer quadrant should be used for intramuscular injections. The insertion of the needle is frequently a source of pain to the patient, although it is not at all necessary. The majority of sensory nerve endings which are likely to be touched with the needle are located in the deeper layers of the skin, not in the fat or tissues immediately below it. To minimize the pain, the skin should be penetrated quickly.

Medications which cause pain upon contact with the tissues should be deposited quickly after aspiration to make sure that the needle is not in a vessel. Slow and gentle injection of such material simply heightens the pain of the process. Intravenous injections are usually almost free from pain if done with good equipment. Most needles become burred and bent after perhaps a dozen uses and sterilizations. The best test for a burr is

done by raking the needle across the alcohol sponge. If the needle picks up cotton, it has a burr which can be an exquisitely painful thing upon intravenous injection.

LACERATIONS

To close a laceration without anesthesia is a torturesome process, yet this is sometimes still done. Many of us administer an anesthetic but put it in the wrong place. Then we begin working too quickly so that the total effect is that of closing a laceration with no obtundation of pain. The important point to remember, once again, is that the sensory nerves being located mainly in the deeper layers of the skin, pain arises principally from closing a laceration in these areas. In injecting a local anesthetic, attempt to spread the solution immediately below the skin with a great deal more thoroughness than in fatty tissue or muscle. The deep fascia has many nerve endings and is second in sensitivity. Muscular tissue would be third and fat last in number of sensory nerve endings. After injecting a local anesthetic wait a minimum of five minutes for it to take effect.

In the closure of lacerations, keep it well in mind that these tissues are going to swell. If a laceration is tightly closed, the stitches are likely to cut and cause much pain. If the edges of the wound are brought very loosely together excellent healing will be obtained in most instances. We tend to use stitches far more often than is necessary. Cellophane tape is being used more and more to close wounds and is often the best way. Occasionally, when we have a rather gaping wound in a very young child, we place a piece of tape on either side of the wound and stitch the *tape* together with no stitches in the living tissue at all. This works just as well as the more painful way of placing the stitches in the skin.

PELVIC EXAMINATION

There are two points of paramount importance. The first is that of gentleness. One gains nothing at all by thrusting a hand into the vagina and rushing through the examination. A rough pelvic examination causes muscle guarding on the part of the patient which will result in major hindrance to the examining physician. Each patient should be instructed in how to cooperate in this examination. I place two fingers in the vagina but make no effort to feel deeper structures. Then by pushing gently on them, I show her the posterior structures of the pelvic sling. She is instructed to let these muscles go so that they can be pushed on without pain. Usually with a little practice, the lady can learn to do this easily. Just to make the point quite clear, she is asked to tense these muscles while I press on them quite firmly. Usually she gives a yelp of pain and looks at me indignantly. This is an excellent time to explain what we mean by relaxing the muscles so that a pelvic examination will not hurt. If you will take time to instruct your patients in the art of cooperating during a pelvic examination and then will make your manipulations most gentle, the information gained from the examination will be greatly increased.

RECTAL EXAMINATION

Intense pressure on the rectal sphincter is painful, but slow, steady and gentle pressure will gain quick penetration. The gloved finger should be placed in the very center of the anus and pushed firmly but gently in

the direction of the umbilicus. Once penetration is made, the finger should be held still for a moment before attempting a wide, sweeping exploration. This will give the sphincter opportunity to relax further and will allow the patient a moment to reflect on the fact that the procedure is not necessarily painful. As in all other manipulations, gentleness is the keynote. It is impossible to do a satisfactory rectal examination on a patient who has been hurt only a few seconds before. Hard pressure on the prostrate in males is painful and should be avoided if at all possible.

EMOTIONAL PAIN

Casual statements made without thinking or with insufficient explanations can cause great difficulty for the patient. Each of us runs the risk of establishing a permanent psychoneurosis in every patient we see, and this risk should be duly considered in talking with patients. However, that is a big subject in itself and one perhaps for a separate article.

CONCLUSION

These examples have been a rather quickly selected series of procedures which can be done more gently and with less pain than is usually the case. We all have a tendency to become somewhat careless about causing pain. It is a tendency we should guard against with every means at our command. Any patient is deeply grateful to the doctor who will eliminate as much pain as possible from the techniques of practice.◄

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EATON LABORATORIES, NORWICH, NEW YORK

ORIGINAL ARTICLE

Use of Hydroxyzine Pamoate* in the Treatment of Pruritus

Pruritic symptoms were relieved by hydroxyzine in 70 of 77 patients with various common skin disorders

RALPH BEHLING, M.D.,† *San Mateo, California*

In the 1959 edition of the Physicians' Desk Reference some 283 agents are offered for the treatment of dermatoses. Generally speaking, these agents fall into four categories:

1. Antihistaminics.
2. Ataractics or tranquilizers.
3. Cortico-steroids.
4. Analgesics.

New agents for the relief of pruritus are being introduced at the rate of one or more per month. Nevertheless there is still a need for an effective agent for the treatment of dermatologic conditions and relief of pruritus.

It has long been established that emotional stress has a definite part in the production of dermatoses such as neurodermatitis, atopic dermatitis, urticaria, pruritus ani, pruritus vulvae, lichen planus, psoriasis, and seborrheic dermatitis, and that aids to emotional balance contribute greatly to a favorable clinical course in these conditions. Drugs previously used for this purpose have had various disadvantages ranging from habit formation, somnolence, and the rapid development of toleration, to the recently reported blood dyscrasias, jaundice, parkinsonism, and drug rashes.

*Vistaril®, Pfizer Laboratories, Brooklyn, New York.
†University of California School of Medicine, Division of Dermatology.

TABLE 1

RESULTS WITH HYDROXYZINE PAMOATE AS PRIMARY THERAPY

	Excellent	Good	Fair	Poor	Total
Lichen Simplex Chronicus	1	1			2
Atopic Dermatitis	1				1
Neurodermatitis	9	4		1*	14
Pruritus Vulvae	4†				4
Pruritus Ani	7				7
Generalized Pruritus	1				1
Insect Bites	1				1
Hodgkin's Disease (pruritus secondary to)	1				1
Obstructive Jaundice (pruritus secondary to)	1				1
Urticaria	1				1
Seborrheic Dermatitis	1				1
Totals	28	5	—	1	34

*25 mg. b.i.d.
†One case of five years duration

Other side effects such as headache, nausea, vertigo, nasal congestion and depression frequently have been observed and, on occasion, have necessitated withdrawal of these drugs.

The clinical data available reporting the use of hydroxyzine in both the hydrochloride and pamoate salt formulations indicates that the most serious side effect resulting from hydroxyzine therapy was a measure of diurnal somnolence, which was usually of a transient nature. The antihistamines have been used widely in the treatment of pruritus, for their specific activity against histamine-induced pruritus, and their sedative or ataractic activity. Excellent results have been reported from the use of the cortico-steroids as well as antipruritics, but the systemic use of these compounds requires very careful supervision to minimize undesired effects.

Hydroxyzine has been classified as a psychotherapeutic antihistaminic drug.[1] Inasmuch as both antihistaminic and ataractic drugs have demonstrated their usefulness in the control of pruritus, the combination of antihistaminic and ataractic activity in hydroxyzine suggested its usefulness as an antipruritic. For this study, the pamoate salt of hydroxyzine* was chosen. Pamoic acid is a physiologically inert compound which has been used to render other compounds, particularly the water-soluble compounds, insoluble and hence more stable. There are two advantages to a less soluble salt of any given drug: longer drug activity with a general leveling of the "peak and valley" pattern of highly soluble salts, and tastelessness of the compound, important because some regurgitation is common with any orally administered drug.

METHOD OF STUDY

In this study, 77 patients suffering from 25 common dermatologic disorders were treated. These cases fell generally into two groups, in which pruritus was treated with hydroxyzine as primary therapy (Table 1) or as an adjunctive therapy (Table 2).

Sixty-four of the 77 patients received 50 mg. of the drug one to two

1. A.M.A. Council on Drugs, *J.A.M.A.*, 166:1040, 1958.

*Vistaril Capsules, Pfizer Laboratories, Brooklyn, New York.

TABLE 2

RESULTS WITH HYDROXYZINE PAMOATE AS ADJUNCTIVE THERAPY

	Excellent	Good	Fair	Poor	Total
Acne	2				2
Tinea	1				1
Infantile Eczema	1				1
Hand Eczema	3	1	1*		5
Drug Eruption (Thyroid)	1				1
Psoriasis	2	2		2*	6
Herpes Simplex		1			1
Contact Dermatitis	8			1*	9
Contact Dermatitis (Poison Oak)	2			2*	4
Stasis Dermatitis		1			1
Seborrheic Dermatitis	1	1*		1*	3
Folliculitis	1				1
Lichen Planus		1			1
Pityriasis Rosea	2	2			4
Verruca Planae	3				3
Totals	27	9	1	6	43
Over-All Results (Tables 1 & 2)	55	14	1	7	77

*25 mg. b.i.d.

times daily. Of the remaining patients, three received 50 mg. three times daily, nine 25 mg. twice daily, and one 25 mg. four times daily. The period of treatment was from 4 to 30 days.

Patients who obtained complete or almost complete remission of symptoms were rated as having excellent results; marked and fair to moderate improvement was designated "good"; little or no change in patient status, "poor." In the cases of the patients in Table 2, who received the compound as adjunctive therapy, decrease in the subjective complaints was considered improvement, even though no significant change occurred in the basic pathology. In 34 cases where the drug was used as the primary medication, evaluation was made on the basis of both subjective and objective criteria.

The pruritus of the 77 patients remitted to an excellent degree in 55 cases, a good degree in 14 cases, and a fair degree in one case. Seven cases were considered therapeutic failures. All of the patients exhibiting a poor or fair response were on a dosage schedule of 25 mg. given twice daily. The failures occurred early in the study when hydroxyzine was given in too small a dosage.

In the treatment of seven patients with pruritus ani and four with pruritus vulvae, excellent results were obtained in all cases, even though one patient's severe pruritus vulvae was of five years duration and had failed to respond to previous therapy, and several patients with pruritus ani had been treated unsuccessfully for periods in excess of one year.

Several patients complained early in the course of treatment of drowsiness for 24 to 72 hours. This was not necessarily an indication for a reduction in dosage. In only one of the 77 patients was it found necessary to discontinue the treatment because of diurnal somnolence.

DISCUSSION AND SUMMARY

A dosage of 50 mg. given twice daily should be considered the minimum starting dose. The high level of

toleration and the infrequency of side effects permit increase of dosage as required—to as much as 100 mg. four times daily.[2,3]

Of the reported cases, 75 were seen in the office and two were hospitalized — one with Hodgkin's disease, the other with obstructive jaundice, both suffering from a generalized secondary pruritus. These latter were each given 50 mg. of hydroxyzine pamoate twice daily, and complete remission of the pruritus resulted within 24 hours in both instances. An interesting aspect of these two cases is that the freedom from side effects and the level of safety inherent with the drug makes it suitable for use in the presence of serious chronic disease, either as an ataractic or an antipruritic medication.

Seventy-seven patients were treated with hydroxyzine pamoate for four days to 30 days in dosages of 25 mg. twice daily to 50 mg. three times daily. Excellent results were achieved in 28 patients with pruritus as the primary complaint. An additional five patients exhibited a good result and one patient a poor response.

In the remaining 43 cases in which the drug was used as adjunctive therapy, 27 patients achieved excellent results; nine achieved good results; one achieved a fair result, and the results were poor in six cases.

Of the 77 patients treated, seven therapeutic failures resulted. In 70 cases, the pruritic aspect of the patient's disease was either controlled or markedly decreased with administration of hydroxyzine pamoate.◀

2. Ayd, F. J., Jr., *New York J. Med.*, 57:1957.
3. Ayd, F. J., Jr., International Symposium on Psychotropic Drugs, Milan, Italy, 1957.
4. Selected Materials on Environmental Aspects of Staphylococcal Disease, *Public Health Service Publ.* No. 646, 1959.

ORIGINAL ARTICLE

Personality and Placebo Response in Hay Fever Patients

Results in 37 hay fever patients treated with an antihistamine and a placebo indicate that personality does not greatly influence response

MAYER A. GREEN, M.D., F.A.C.A.,* *Pittsburgh, Pennsylvania*

There is general belief that hay fever is one allergy in which the role of emotions is minimal. The basis for this belief is the usually high correlation seen between severity of symptoms and the pollen count. On the other hand, there are factors which cause one to wonder whether or not the psychic element in hay fever is more important than is generally supposed in influencing the patient' response to antigens and to medication. The report of a rose fever patient sneezing in the presence of a paper rose is now a textbook commonplace.[1] If rose fever contains this element of suggestibility, there would seem to be some question whether a hay fever victim might not be just as suggestible, either to external stimuli or to medication.

With this question in mind, this study was undertaken with two objectives: first, to observe whether hay fever patients are as subject to placebo response as other patients; second, to observe whether stability of personality significantly influences their response. In order to determine de-

*Clinical Assistant Professor, Allergy Section, Department of Dermatology, University of Pittsburgh School of Medicine. Senior Physician, Department of Medicine, Chief of Allergy, Columbia Hospital, Pittsburgh. Senior Physician, Department of Medicine, Division of Allergy, Montefiore Hospital, Pittsburgh.

1. Urbach, E., & Gottlieb, P. M., Allergy, Grune and Stratton, New York, 1943, p. 89.

gree of emotional stability, a psychological test was included in this study plan.

MATERIAL AND METHOD

Forty-three patients suffering from ragweed hay fever were originally surveyed in the series. This number was reduced to 37 in the final tabulation when 6 patients were excluded because they did not complete successive courses on placebo and antihistamine. The patients were aware that they were taking part in a study and that all capsules were not the same; most were interested and cooperative. The usual symptoms of itching, burning eyes, nasal discharge or congestion, and sneezing were present in moderate to marked degree in spite of hyposensitization. The group was fairly representative of hay fever patients in my practice, being about equally divided with regard to sex and showing a wide age range from 19 to 73 years. All had chronic hay fever, some for as long as 25 years.

Psychologically, the patients in this series provided quite a cross section, varying from highly stable persons on the one hand to extremely neurotic persons on the other. All patients took the Cornell Index[2], a psychological test designed to reveal the presence of anxiety states, hypochondriasis, and other emotional instabilities. The present form, N2, is a direct descendant of Form N which was used extensively for military psychiatric screening. This test can be administered and scored in a short time and requires no psychological training to interpret. It contains 101 questions, which fall into two groups: those differentiating sharply between persons with serious personality disturbances and persons without such disturbances, (e.g., "Does worrying continually get you down?"); and those having to do with significant bodily symptoms, (e.g., "Do your stomach and intestines work badly?"). Seventeen of the 37 patients received scores on the psychological test identifying them as emotionally unstable. The test scores also provided some insight into the nature of the patients' emotional difficulties, revealing such things as schizoid personalities, depressive tendencies, and anxiety reactions. Some of these personality problems were already familiar to me from past interviews and long knowledge of the patient; in other cases, the test provided some surprising results which were confirmed in the course of further interviews.

All patients were studied for four weeks at the peak of the 1958 hay fever season. Thus the major external variable, the pollen count, was distributed over the entire group and favored neither drug nor placebo response. Each patient was given a coded envelope containing a week's supply of a clinically useful antihistaminic drug (Teldrin) or an identical placebo capsule. Neither the patient nor I knew which capsule was being given; my office aide distributed the medications according to a plan designed to permit a statistical analysis of the responses obtained. In the course of the four weeks, patients were to receive alternately the placebo and the active medication. Some were started on the placebo, some on the antihistamine. They were told to take one capsule in the morning and one before going to bed at night. Each patient was given a daily report

2. Weider, A., et al., *Psychosom. Med.*, 8:411-413, 1946.

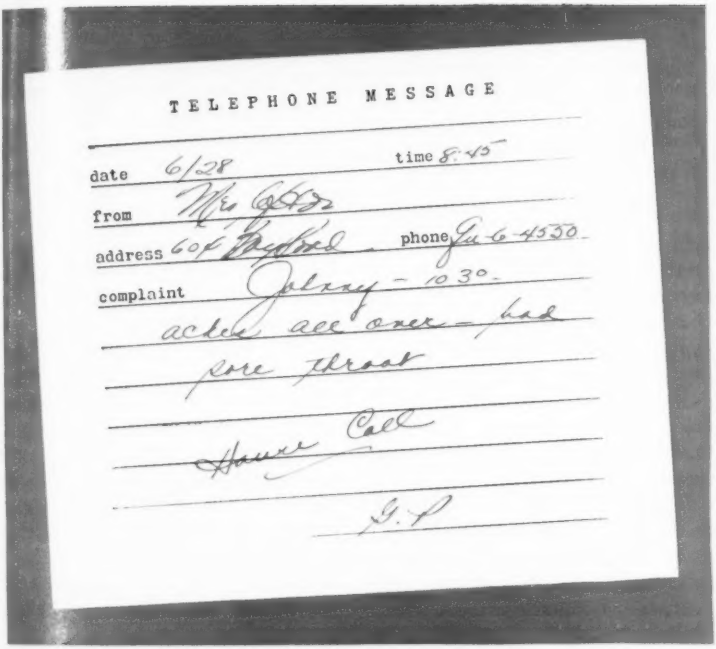

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TABLE 1

RELATIONSHIP BETWEEN STABILITY OF PERSONALITY AND RESPONSE TO MEDICATION IN 37 PATIENTS

TYPE OF PERSONALITY	NUMBER OF PATIENTS RESPONDING TO PLACEBO	NUMBER OF PATIENTS RESPONDING TO ANTIHISTAMINE	TOTAL PATIENTS
Stable	5 (25%)	15 (75%)	20
Unstable	6 (35%)	11 (65%)	17
TOTAL	11	26	37

card to fill in at the end of each day of treatment; in this manner, dependence on memory was minimized. On this card, patients recorded with a simple check mark the severity of symptoms, dosage taken, and any side effects noted. These cards were returned to me each week. Inevitably, there were a few patients who filled out their cards in the waiting room, thus defeating my purpose, but most of the patients filled out the reports each day. In addition, I kept patient charts listing symptoms, pertinent history, dosage, estimate of severity of symptoms at each visit, coded capsule number administered at each visit, side effects reported, and any comments volunteered by the patient.

RESULTS

Eleven patients (30%) showed some degree of response to the placebo: of these, seven obtained equal benefit from placebo and antihistamine and four reported better symptomatic relief from the placebo. This 30% represents a higher degree of placebo response than would be generally expected and comes close to the 35% average noted in such conditions as wound pain, angina pain, anxiety states, and the common cold.[3] As to stability of personality, five were stable and six were unstable. Table 1 illustrates the incidence of placebo response in each group. Just as some experienced benefit from the placebo, so also did several patients experience side effects. Two patients reported drowsiness from the placebo but not from Teldrin, while two others reported side effects from both the medication and the placebo. Of these four patients, two were emotionally unstable and a third would have to be considered as bordering on the unstable category by virtue of her high score on the Cornell Index. (Her score was 12; a score of 13 or over indicated an unstable personality.)

Twenty-six patients (70%) received better symptomatic relief from the antihistamine. This difference between response to Teldrin and placebo is statistically significant. ($P<.01$). Although Teldrin produced measureably better relief than the placebo, it produced no significantly higher incidence of side effects. Three patients reported side effects from the medication, while two patients reported similar side effects from the placebo. Two others reported similar side effects from both placebo and antihistamine. The low incidence of side effects, especially drowsiness, proved useful in this study in preventing either the patient or myself from breaking the code. In general, therefore, the antihistamine was effective and excep-

3. Beecher, H. K., *J.A.M.A.*, 159:1602-1606,1954.

tionally well-tolerated.

The emotional make-up of the individual did not appear to have any significant influence on response to therapy. Results in the 17 patients with unstable personalities were not very different from those observed in the more stable (See Table 1.) Eleven of the seventeen (65%) benefited from the antihistamine as compared to 15 of the 20 (75%) in the emotionally stable group. This difference is not significant statistically. However, the unstable patients did tend to be more prone to side effects, or at least to the reporting of them. Six of the 7 patients who reported side effects from either medication were unstable.

Despite the conclusion that personality does not greatly influence response to hay fever treatment, it must be admitted that there are individual patients whose anxiety is so acute as to aggravate physical symptoms. Their prognosis is always poor until this acute anxiety state is relieved. One of the least satisfactory responses seen in this study, for example, was that of a woman of 60. This patient was extremely anxious and made a number of complaints. She at first objected to taking part in this study and then tearfully begged to be included. She had been under specific hyposensitization therapy for three years with generally favorable results, but complained that this year was "the worst ever." Pollen counts were not especially high this season and she continued to have moderately severe symptoms even when the count was low. It seems likely, therefore, that her anxious state of mind played some part in her lack of response to therapy.

SUMMARY

Thirty-seven ragweed hay fever patients were given a psychological test and then received successive courses on identical capsules containing a placebo or an antihistamine (Teldrin). This study was carried out to observe the degree of placebo response in hay fever patients and to observe whether stability of personality influenced this response.

Eleven patients (30%) showed a placebo response as compared to an average of 35% in most disorders. Of the 11, 5 were stable and 6 unstable. Twenty-six patients (70%) received better relief from the antihistamine. Among emotionally unstable patients, 11 of 17 (65%) benefited from the antihistamine, 6 of 17 (35%) from the placebo. Among the more stable patients, 15 of 20 (75%) benefited from the antihistamine and 5 of 20 (25%) from the placebo. Stability of personality appeared to have only a slight effect on patients' response to medication but seemed to play some part in side effects, or at least in the reporting of them. Six of the seven patients reporting side effects were emotionally unstable.◀

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WHENEVER A DIAPHRAGM IS INDICATED

ORIGINAL ARTICLE

Relief of Muscle Spasm with Two Chlorzoxazone Preparations

No gastrointestinal disturbances were reported, and the beneficial effect was frequently manifested within an hour of administration

EDWARD SETTEL, M.D., *Forest Hills, New York*

Progress in the development of new drugs with the capacity to reduce tonicity of striated muscle was stimulated in 1946 by a report on the muscle-relaxant action of mephenesin.[1] Subsequently, mephenesin carbamate, zoxazolamine, meprobamate, methocarbamol, and styramate have been introduced. Among these compounds, zoxazolamine* was the first to manifest significant muscle-relaxant action when administered orally. Clinical reports[2-8] appear to confirm the impression that it is probably the most effective agent of the group for the treatment of striated muscle spasm due to causes other than disease of the central nervous system. As is so often the case with potent therapeutic agents, side effects sometimes reduce the clinical usefulness of zoxazolamine. However, it has been possible to minimize the side effects by giving the drug with food or as an enteric coated tablet. A synthesized analogue of zoxazolamine has

*Flexin,® McNeil Laboratories, Philadelphia.

1. Berger, F. M., & Bradley, W., *Brit. J. Pharmacol.*, 1:265,1946.
2. Amols, W., *J.A.M.A.*, 160:742,1956.
3. Smith, R. T., et al., *J.A.M.A.*, 160:745,1956.
4. Abrahamson, E. H., & Baird, H. W., III, *J.A.M.A.*, 160:749,1956.
5. Rodriguez-Gomez, M., et al., *J.A.M.A.*, 160:752, 1956.
6. Smith, R. T., *J. Am. Geriatrics Soc.*, 5:152,1957.
7. Johnson, H. J., Jr., *Am. Pract. & Digest Treat.*, 8:1558,1957.
8. Settel, E., *Am. Pract. & Digest Treat.*, 8:443,1957.

been given the name chlorzoxazone.* This agent is rapidly absorbed from the gastrointestinal tract, peak plasma levels being reached in 1-3 hours, and a significant concentration maintained for six hours or more.[9] The average plasma level is 2 to 5 times that achieved by a comparable dose of the parent compound zoxazolamine. In a comparative study in animals,[10] chlorzoxazone exceeded in both potency and duration of action the mephenesin group of drugs and compared favorably with zoxazolamine itself.

The clinical use of chlorzoxazone was studied in a small group of patients with low back pain, osteoarthritis, and post-traumatic myofascitis. In this preliminary double-blind study, good to excellent results were obtained in 14 of the 15 patients. No blood, renal, or hepatic abnormalities appeared, and no side effects were observed.

As with zoxazolamine, the new drug has manifested its greatest effectiveness in skeletal muscle spasm arising from orthopedic and arthritic disorders, and is less consistently of value in spasm arising from central nervous system pathology. In the former group of disorders it was generally found desirable to prescribe, in addition to chlorzoxazone, acetaminophen,† an analgesic for added relief from pain, and in some instances one of the corticosteroids for anti-inflammatory effect. The obvious convenience that would be derived from being able to prescribe such combined therapy in one preparation prompted a study of two combination preparations.*† In both, the quantities of active principle were those considered optimal for most patients. The steroid dosage is in line with the current trend toward lower doses of these useful but potent agents.

MATERIALS AND METHOD OF STUDY

Depending on the patient's age and weight and on the severity of the condition, either tablet was administered in a dosage of 1 q.i.d. or 2 q.i.d. and continued at this level until symptoms subsided. If there was little or no change after 3 to 4 weeks of treatment, the results were considered poor and the medication withdrawn. In the case of the preparation with prednisolone, withdrawal was made slowly, whereas, with the other preparation, the drug was discontinued abruptly. Where there existed chronic disease such as osteoarthritis, maintenance for an indefinite period often proved satisfactory on a dosage of 1 tablet b.i.d. or t.i.d. The two types of tablets were administered at random, with the exception that preference was shown for the prednisolone preparation in cases of rheumatoid arthritis because of the steroid content. No contraindications were observed except that the prednisolone preparation was not used in any patient in whom steroid was considered inadvisable.

SELECTION OF PATIENT

A total of 62 patients was placed under observation. Of these, 47 were drawn from private practice in an urban community, and 15, ranging in age from 61 to 85, were patients of a nursing home and rehabilitation

*Paraflex,® McNeil Laboratories, Philadelphia.
†Tylenol,® McNeil Laboratories, Philadelphia.
9. Conney, A., et al., *Fed. Proc.*, 17:360,1958.
10. Unpublished Data. Pharmacology Department, McNeil Laboratories, Inc., Philadelphia.

*Parafon,® McNeil Laboratories, Philadelphia, is composed of chlorzoxazone 125 mg., and acetaminophen 300 mg.
†Parafon with Prednisolone,® McNeil Laboratories, Philadelphia, is composed of chlorzoxazone, 125 mg., acetaminophen 300 mg., and prednisolone 1 mg.

TABLE 1.

DIAGNOSIS REPRESENTED IN TREATMENT GROUP OF 62 PATIENTS

DIAGNOSIS	TREATMENT	
	PARAFON WITH PREDNISOLONE	PARAFON
Acute low back syndrome (with or without sciatica)	10	5
Trauma (injury to joint or periarticular structures)	5	2
Rheumatoid arthritis (acute episode)	9	1
Exacerbation of recurrent osteoarthritis	6	6
Myositis (primary) and/or tendinitis	6	3
Bursitis (acute calcific)	3	0
Acute torticollis	3	1
Recurrent neuritis	1	0
Hemiplegic contracture (subacute)	1	0
TOTALS	44	18

center. Among the total group there were 18 males and 44 females. The age distribution was as follows:

AGE GROUP	NUMBER OF PATIENTS
14 - 30	6
31 - 40	6
41 - 50	14
71 - 80	17
61 - 70	6
71 - 80	12
81 and over	1
Total	62

Since the only criterion for selection of patients was the existence of voluntary muscle spasm not due to C.N.S. disorder, a variety of diagnoses was represented in the treatment group as shown in Table 1.

RESULTS

Results were tabulated according to the degree of clinical improvement manifested by relief of pain, reduction of spasm, and increase in range of motion. They were classified as excellent when relief was complete within the first or second week of therapy; as good when there was measurable, but not complete, relief within one to two weeks; and as poor when symptoms were unaffected or became worse (Tables 2 and 3).

On the basis of these criteria for assessing clinical benefit, both preparations gave a high percentage of good to excellent results. Although double-blind studies with an inactive placebo were not done, it would not be anticipated on the basis of prior experience that more than 30 to 40 per cent would react favorably to placebos. Hence, a good to excellent response in more than 80 per cent of the patients in this study is indicative of therapeutic effect rather than a response to suggestion. In those acute conditions treated, a good or excellent result was not recorded unless recovery and relief of muscle spasm was observed more promptly than would be expected with accepted current methods of treatment.

SIDE EFFECTS

All patients were observed carefully for side effects. Careful questioning revealed no evidence of untoward reactions. Clinically, there was no evidence of rash, vertigo, headache, drowsiness, edema, tinnitus, tremor or gastrointestinal upset. In all patients, urine analyses, blood counts, renal and hepatic profiles,

TABLE 2.

RESULTS OF TREATMENT WITH *PARAFON WITH PREDNISOLONE*

DIAGNOSIS	CLINICAL RESPONSE		
	EXCELLENT	GOOD	POOR
Acute low back pain	8	2	0
Trauma	3	2	0
Rheumatoid arthritis	7	1	1
Osteoarthritis	0	4	2
Myositis	4	1	1
Bursitis	1	0	2
Torticollis	1	2	0
Neuritis	0	0	1
Hemiplegia	0	0	1
TOTALS	24 (55%)	12 (27%)	8 (18%)

TABLE 3.

RESULTS OF TREATMENT WITH *PARAFON*

DIAGNOSIS	CLINICAL RESPONSE		
	EXCELLENT	GOOD	POOR
Acute low back	3	2	0
Trauma	2	0	0
Rheumatoid arthritis	0	0	1
Osteoarthritis	2	2	2
Myositis	1	2	0
Torticollis	1	0	0
TOTALS	9 (50%)	6 (33%)	3 (17%)

conducted both before and after treatment, failed to reveal any adverse changes that could be attributed to the medication.

COMMENTS AND CONCLUSIONS

The results achieved in this study indicate that chlorzoxazone is a potent skeletal muscle relaxant, that, when used in conjunction with acetaminophen or acetaminophen and prednisolone, affords good to excellent relief of painful skeletal muscle spasm in more than 80 per cent of the cases treated. The beneficial effect of these drugs is frequently manifested within an hour of administration and the effect of a single dose lasts about six hours. Experience of continued administration over a period of months in a few chronic cases indicated that the drug retains its effectiveness indefinitely. The dosage of either preparation usually need not exceed two tablets three or four times a day.

In this series of cases no side reactions of any nature were observed. The absence of gastrointestinal disturbance was gratifying.◀

ORIGINAL ARTICLE

A Psychopharmacologic Approach to Weight Reduction

By controlling emotional disturbances and reducing blood pressure, weight loss was achieved in a group of 20 obese, highly emotional patients

CHARLES A. LAPIN, M.D., and MOREY LAPIN, M.D.,
Beverly Hills, California

Although most obesity is the result of a caloric intake greater than the energy expended, there is the occasional patient with a true endocrine disorder, and also a group whose obesity is primarily a result of emotional tension.

In the latter group, the percentage of patients successfully treated is usually quite small. To this type of patient, eating is a source of emotional satisfaction, and not just a physiologic desire. Even the thought of having to go on a diet, in spite of the patient's intellectual acceptance of the need for weight reduction, can produce a marked anxiety. On the usual routines, these patients may lose some weight, but only to a point, and then fail to continue because of a lack of the feeling of well-being.

Because of these considerations a study was done to determine the possible value of a combination of reserpine and methylphenidate hydrochloride*, a CNS stimulant, in controlling these emotional disturbances. It was hoped that by gaining such control, weight loss would be achieved in spite of the fact that neither of the compo-

*Serpatilin®, Ciba Pharmaceutical Products, Inc., Summit, N. J.

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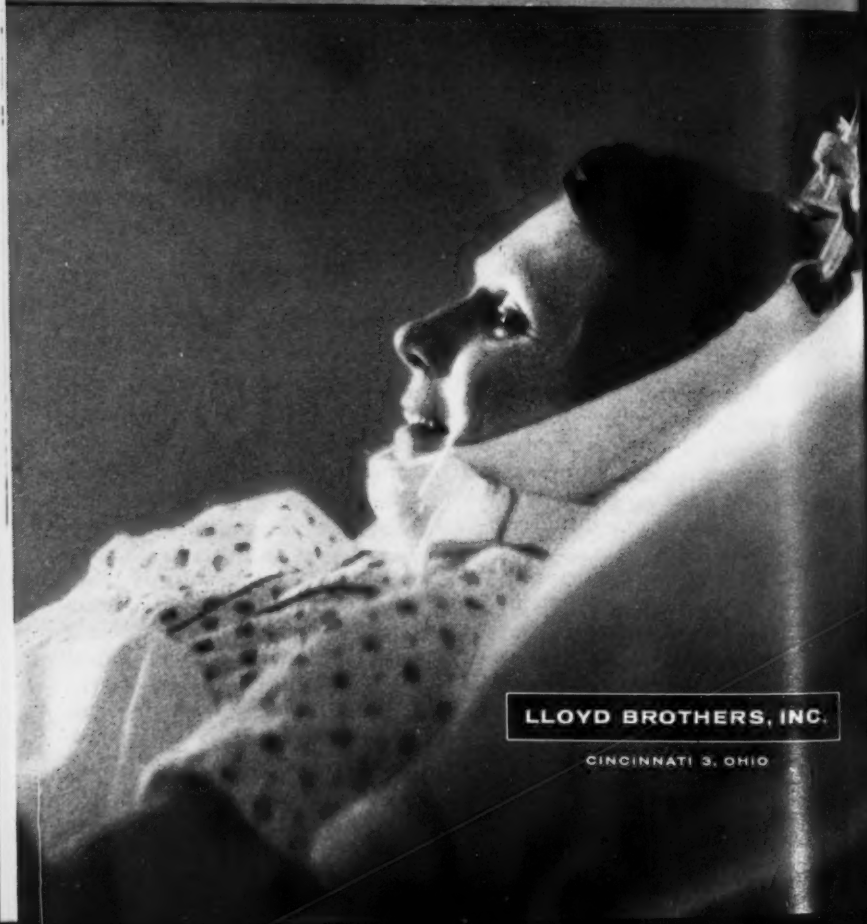
DOSAGE: For adults and children over 12, one or two capsules. For children, age 6 to 12, one capsule. Administered at bedtime for 2 or 3 days or until bowel movements are normal. Supplied in bottles of 30 and 100 soft gelatin capsules.



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nents of the drug are appetite suppressants.

In fact, reserpine has listed as one of its side effects weight gain and has been used to help patients put on weight.[1] The other part of the combination, methylphenidate hydrochloride*, although a central nervous system stimulant, is not an appetite suppressant.[2]

STUDY

Twenty patients, all of whom were overweight and evidenced emotional tensions were selected for trial. In addition, sixteen of them had hypertension. All of the patients had previously been given some form of anti-obesity therapy which often included, besides the standard dietary restrictions and hormonal therapy, appetite suppressant medications and tranquilizers.

There were 17 women and three men, ranging in age from 25 to 65. Besides the dietary restrictions, patients were given one to three tablets of Serpatilin a day for periods of three to 16 weeks.

RESULTS

All patients succeeded in losing at least five lbs., and one as much as 25 lbs. The average weight loss was 14 lbs., roughly 1-½ lbs. per week. All but one patient with an elevated blood pressure had a satisfactory reduction, including two patients whose initial diastolic pressures were 120 and 140 mm Hg respectively. Those patients whose blood pressure was within a normal range at the start of therapy remained essentially static. However, one hypertensive patient who did not have any significant reduction in blood pressure did successfully take off 18 lbs. in weight in seven weeks. It may be that on continued therapy his blood pressure will be reduced, or it may be necessary to add further anti-hypertensive medication.

One patient was put on Serpatilin for a period of six weeks. She lost weight, and her blood pressure was reduced from 180/90 to 150/80. She was taken off the medication for a period of four weeks. During this period, her blood pressure returned to 160/90 and the weight reduction ceased. On reinstitution of treatment, the blood pressure returned to 150/80, and weight reduction resumed.

SIDE EFFECTS

There were no side effects, probably because the dose of reserpine was kept low (each tablet contains only 0.1 mg.) and thus the maximum dose per day was 0.3 mg. of reserpine. It also may have been related to the combination of the drugs. Methylphenidate hydrochloride has been reported to successfully overcome lethargy due to tranquilizers and other sedatives, and also has been said to cut down the amount of nasal stuffiness. Regardless of the reasons, no patient had to be taken off the medication.

DISCUSSION

Naturally, some patients can reduce on other medications, but it is interesting to note that in this group of patients the preparation had to be added to the other medications or routine in order to acquire the desired weight reduction.

Some of the hypertensive group, who had been on reserpine and

*Ritalin,® Ciba Pharmaceutical Products, Inc., Summit, N. J.

1. Diukin, L. D., Use of Rauwolfia in Treatment of Malnutrition. New York Scientific Exhibit, New York Medical Society Meeting, Feb. 18-21, 1957.
2. Ferguson, J. T., & Funderburk, W. H., *J.A.M.A.*, 166:259,1958.


Dimetane works in all symptoms of allergic rhinitis; and in urticaria, atopic and contact dermatitis. The summary conclusion of extensive clinical studies to date: Dimetane provides unexcelled antihistaminic potency with minimal side effects.
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weight reducing medication, reduced only to a point, but then lacked the sense of well-being needed to persevere. Some of the referrals, who had "tried everything" were about to give up. Further weight reduction was accomplished only after the reserpine - methylphenidate hydrochloride combination was substituted, and their attitudes then showed marked improvement. The drug combination had a lasting effect in contrast to the short action of amphetamine, which should not be used in hypertensives. There did not seem to be the let-down phenomena often seen with amphetamines.

SUMMARY

A group of 20 obese, highly emotional patients, 16 of whom were hypertensive, were given a combination of reserpine and methylphenidate hydrochloride to determine if it would control their emotional disturbances and their weight. This routine enabled them to successfully lose weight, and lowered the blood pressure of all but one hypertensive patient. All patients had ceased to lose weight, or had been unable to lose weight on previous routines and medications.◀

Acquired Esophagotracheal Fistula Secondary to a Body in the Esophagus

A soldier of 19 stated that three months previous to hospitalization, after an epileptic seizure, he was unable to find his denture, a 4-tooth bridge. X-ray study of the chest had given no evidence of radiopaque foreign body. Since that time, he had complained of dysphagia and had gradually lost 30 pounds. During the week before entry he was able to tolerate virtually nothing by mouth.

Attempts to swallow water produced severe coughing. An esophagogram revealed dilation of the first third of the esophagus, with irregular stenosis and marked spasm of the junction of the first and second thirds. Spot films disclosed a fistulous communication between the esophagus and the trachea, with two small, metallic, hook-shaped densities adjacent to the fistulous tract.

Treatment was started with antibiotics and intravenous infusions of fluids. Esophagoscopy revealed a fistula between the trachea and esophagus 5 cm. above the carina. A thoracotomy was then done, and the trachea and esophagus were found to be imbedded in an inflammatory mass in the upper mediastinum. The two structures were separated in this area, and a large fistula was found just above the carina. The opening was partially occluded by a plastic denture 4 by 4 cm. The denture was removed and the openings in the trachea and esophagus repaired, with a flap of pleura interposed.

Recovery was uneventful. An esophagogram three weeks after operation showed some deformity at the operative site, but the barium passed without difficulty and No. 41 bougie was passed readily. He was returned to full duty one month after operation. On a follow-up visit five months later, he had regained lost weight and was asymptomatic except for momentary substernal discomfort on swallowing coarse foods.

Maruyama, Y., et al., *New England J. Med.*, 260: 126-127,1959.

ORIGINAL ARTICLE

Bedside Diagnosis and Treatment of Cardiac Arrhythmias With Rapid Ventricular Rates

The differential diagnosis and emergency treatment of rapid cardiac arrhythmias are discussed

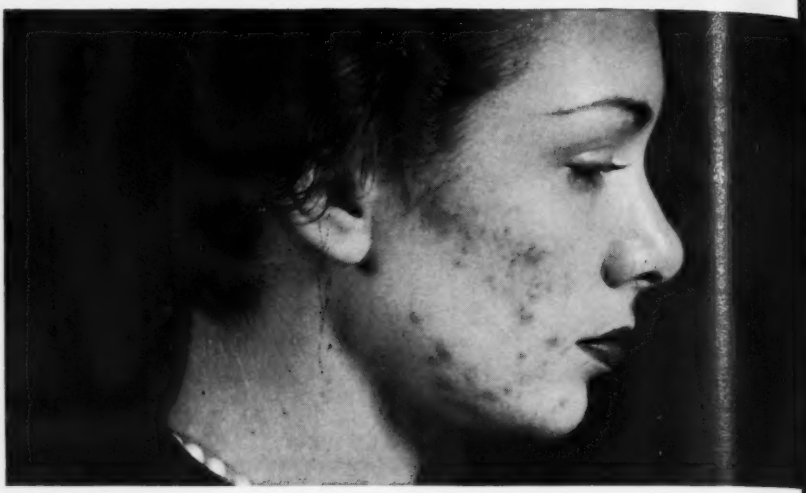
CHARLES FISCH, M.D.,* *Indianapolis, Indiana*

Cardiac arrhythmias often present diagnostic difficulties to the most experienced clinician and electrocardiographer. Fortunately the majority of these arrhythmias are either functional in origin or do not present an immediate therapeutic problem.

There is, however, a group of arrhythmias that by the very nature of the rapid rate may place the patient's life in jeopardy. This group includes atrial and nodal tachycardia, atrial flutter, atrial fibrillation and ventricular tachycardia. Every physician should be able to make a reasonably accurate bedside diagnosis and be able to institute life-saving treatment without electrocardiographic confirmation. The complete diagnosis cannot be reached without a careful history and physical examination. The history should include a thorough inquiry into past medication, especially the use of digitalis. Digitalis has precipitated, at one time or another, every known form of arrhythmia.

The differential diagnosis of the arrhythmias at the bedside must depend to a large extent on the statistical value of the physical findings. Let us assume that the patient has a regular ventricular rate of 220 beats per minute; paroxysmal atrial or

*From the Robert M. Moore Heart Clinic, Indianapolis General Hospital.



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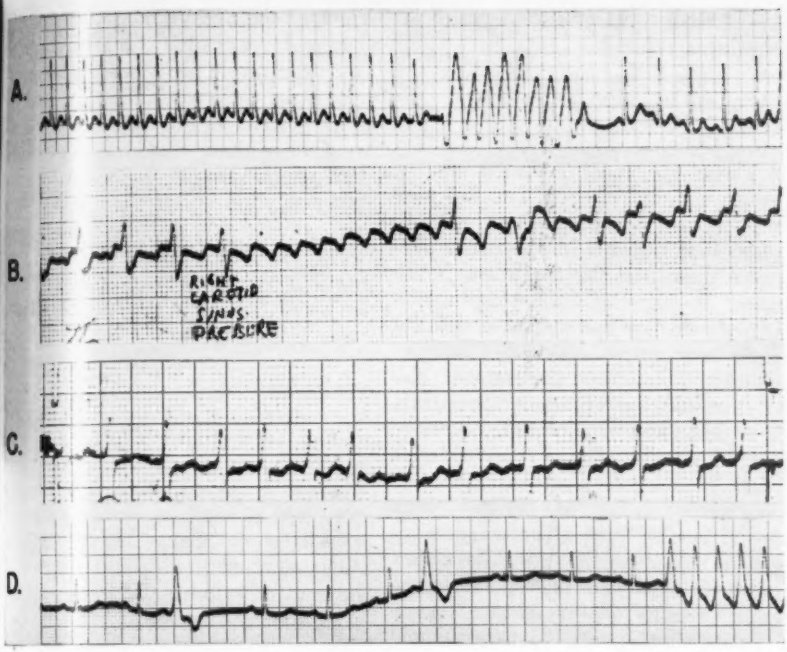


A. Atrial tachycardia with a rate of 200 converted to sinus rhythm by vagal pressure. The unusual feature here is a short run of ventricular tachycardia preceding the appearance of sinus rhythm.

B. Atrial flutter with a 2:1 respond. Carotid sinus pressure increased the degree of block and cessation of vagal pressure resulted in resumption of original rate.

C. Atrial fibrillation. Note absence of P waves (lack of rhythmic atrial contractions) and the grossly irregular ventricular rate.

D. Ventricular premature beats followed by a run of ventricular tachycardia.

nodal tachycardia is the most likely explanation, for very rarely does an atrial flutter and even less commonly ventricular tachycardia attain this rate. The age of the patient, the manner in which the disturbance appeared, the presence or absence of signs of heart disease, and the response to valsalva or carotid stimulation, will allow a reasonably accurate differential diagnosis of the four arrhythmias under consideration.

Some tachycardias appear and disappear spontaneously and may require no treatment. Others persist for hours or days without seriously affecting the patient. As a rule the potential seriousness of the arrhythmia parellels the severity of the associated heart disease and the heart rate. The need for vigorous therapeutic measures is signaled by the appearance of one or more of the following clinical pictures:

1. Shock and anuria due to diminished cardiac output.

2. Angina pectoris due to poor coronary blood flow which may progress and result in myocardial infarction.

3. Congestive heart failure.

We shall consider each form of arrhythmia separately.

PAROXYSMAL ATRIAL AND NODAL TACHYCARDIA

These are most common of the group under discussion. The two may well be considered together, for more often than not it is impossible to separate them and the treatment is the same. Paroxysmal atrial tachycardia is suggested by the sudden onset of a rapid heart rate of 140 to 240, with an average of over 200 per minute. The rhythm of an established tachycardia is regular, and vagal stimulation may not affect the rate or may slow it slightly. Because these arrhythmias frequently occur in persons with sound hearts, the patients may tolerate the rate surprisingly well for hours or even days and the episode may cease abruptly. The usual termination is by a short period of asystole, although auricular fibrillation and ventricular tachycardia have been observed.

Treatment of atrial tachycardia is fairly well standardized. Initially, vagal stimulation should be tried. This may be accomplished by Valsalva experiment, eyeball pressure, pulling on the tongue or gagging. Should these maneuvers fail, which is frequently the case, carotid sinus pressure should be tried—each carotid artery should be pressed separately. If pressure is applied properly a satisfactory result may be expected in 50 per cent of the patients. Should all these measures fail, we administer 0.5 to 1.0 mg. of prostigmine subcutaneously and repeat the vagal maneuvers in 20 to 30 minutes. The next step is administration of 0.6 to 0.8 mg. of digitoxin, which, in combination with repeated vagal stimulation, nearly always terminates the arrhythmia. Occasionally larger doses of digitoxin are required. We very rarely see a case of paroxysmal atrial tachycardia not due to digitalis which does not respond to one or another of these measures. The problem of arrhythmias complicating the pre-excitation syndrome (W-P-W) are complex and outside the scope of this paper.[1] It suffices to state that digitalis may aggravate rather than improve the arrhythmias associated with this syndrome.

ATRIAL FLUTTER

Atrial flutter is practically always a manifestation of a severe form of heart disease, and consequently the patient may find himself in serious difficulty with rates well below 200 per minute. Atrial flutter should be suspected in any patient with heart disease who has a regular rate of 140 to 180 per minute. In an exceptional case of a 1:1 ventricular response the rate may be over 200. Occasionally the rhythm may be irregular because of the changing degree of auriculo-ventricular block. In such instances, in contradistinction to fibrillation, the irregularity will follow a reproducible pattern. The jugular vein may be seen to pulsate rapidly. The diagnosis is almost certain if carotid pressure, by increasing the degree of block, suddenly reduces the rate by one-third or one-half, and with cessation of pressure the rate returns to control levels. Differential diagnosis of atrial tachycardia and the rare case of rapid (200 or over) atrial flutter, especially if the latter fails to respond to vagal stimulation may be impossible at the bedside, and this may be true even after an electrocardiogram is obtained. Fortunately the treatment of either ar-

1. Fisch, C., et al., *Circulation*, 16:1004,1957.

rhythmia is digitalis.

Emergency treatment is directed toward reduction of the ventricular rate. In atrial flutter this can be accomplished with digitalis. Large doses of digitoxin (2 mg. or more) may be required to accomplish the desired degree of AV block. The conversion of flutter to sinus mechanism is rarely an emergency procedure, so any reference to quinidine and pronestyl is omitted.

ATRIAL FIBRILLATION

Atrial fibrillation is a manifestation of organic heart disease. In this condition, as in atrial flutter, the seriousness of the associated heart disease may predispose to severe cardiovascular complications with rates not much above 150 per minute. This arrhythmia is easily diagnosed by the presence of irregular, rapid heart rate, with a pulse deficit and varying intensity of the first heart sound. Only occasionally will an extremely rapid atrial fibrillation give an illusion of regularity.

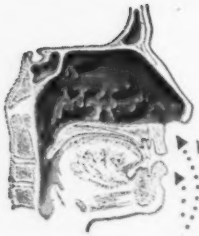
The treatment of choice is digitalis. Slowing of the ventricular rate can be attained in most patients. If one fails to slow the ventricles, the presence of "high output" failures such as thyrotoxicosis, anemia myocarditis and, rarely, beri-beri should be suspected. As in atrial flutter, the conversion of the fibrillation to sinus rhythm is never an emergency and will not be discussed here.

VENTRICULAR TACHYCARDIA

This rare form of cardiac arrhythmia represents a true medical emergency, comparable to diabetic coma or massive and persisting gastrointestinal hemorrhage. This condition should be suspected whenever severe heart disease, especially recent myocardial infarction, is complicatd by the sudden appearance of a ventricular rate of 150 to 180 per minute. The beat is regular or slightly irregular, giant "A" waves may be seen over the jugular vein, auscultation reveals a changing intensity of the first heart sound, and vagal stimulation has no effect on the rate. The tachycardia is often followed by shock with anuria and/or congestive heart failure.

The problem of treatment is complicated by difficulty in establishing an accurate diagnosis. The electrocardiographic pattern of many of the supraventricular tachycardias with aberrant conduction or a pre-existing intraventricular conduction defect has been confused with ventricular tachycardia. Once the diagnosis is made or seriously suspected we administer quinidine. The use of quinidine is never justified unless the physician is familiar with all the pharmacological properties of the drug, its indications and contraindications.

In treating ventricular tachycardia we prefer the intravenous route. Quinidine gluconate 0.8 gm., is diluted in 150 cc. of saline and administered over a period of 30 to 54 minutes. The physician remains at the bedside watching for any side effects or changes in rhythm. Changes in rhythm are immediately checked electrocardiographically. The ECG remains connected to the patient throughout the infusion. The dose may be repeated in one to two hours. When the condition is such that quinidine by mouth is used, the treatment is started with 0.2 gm. of the drug every two hours for five doses. The same plan is followed each day with an increase by 0.1 gm. per dose on each successive day. Rarely is it justifiable to give more than 0.7 gm. every



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References: 1. Sheldon, J. M.: Postgrad. Med. 14:465 (Dec.) 1953. 2. Hubbard, T. F. and Berger, A. J.: Annals Allergy p. 350 (May-June) 1950. 3. Kline, B. S.: J. Allergy 19:19 (Jan.) 1948. 4. Goodman, L. S. and Gilman, A.: Pharmacol. Basis Ther., Macmillan, New York, 1956, p. 532. 5. Fabricant, N. D.: E.E.N.T. Monthly 37:460 (July) 1958. 6. Lhotka, F. M.: Illinois M.J. 112:259 (Dec.) 1957. 7. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958.

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two hours. It is obvious that such a schedule of therapy precludes the existence of an emergency situation.

Intravenous quinidine has been administered to many patients with gratifying results. We do not hesitate to recommend this form of treatment, provided one is familiar with the drug and administers it under electrocardiographic control.

SUMMARY

1. A brief outline of bedside diagnosis and emergency treatment of rapid cardiac arrhythmias is presented. Some of the statements regarding therapy may seem arbitrary. They are, however, based on combined experience of those responsible for the management of the large number of such patients admitted to our hospital and are in agreement with the procedures followed in many other institutions.

2. Digitalis is the treatment of choice in the management of emergency situations arising from all forms of supraventricular tachycardia, except in those cases where digitalis itself is responsible for the arrhythmia. The drug should be administered by mouth. It is a rare situation where the use of intravenous digitalis preparations is justifiable. In such cases the physician must assume the calculated risk of the route of administration as against the possible disastrous effects of continuing tachycardia.

3. In our experience, quinidine is the treatment of choice for ventricular tachycardia.◀

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ORIGINAL ARTICLE

Tic Douloureux: Treatment with Diphenylhydantoin

Diphenylhydantoin afforded pain relief in approximately 50 per cent of patients who had not been relieved by other means

JOSEPH F. DORSEY, M.D., GORDON W. HAYSLIP, M.D., and KITTRIDGE ANDERSON, M.D.,* *Boston, Massachusetts*

Tic douloureux or trigeminal neuralgia is more apt to afflict the elderly. In some cases the affliction will be mild for long periods of time, in other cases there will be exacerbations and remissions lasting over periods of weeks or months. The term tic douloureux is usually reserved for that painful condition characterized by severe, spasmodic, lancinating pains in any one or more of the three divisions of the trigeminal nerve, and which is so often set off by a "trigger point or zone" that may be located anywhere about the face.

*From the Department of Surgery, Division of Neurosurgery, Saint Elizabeth's Hospital, and Tufts University School of Medicine.

ETIOLOGY OF FACIAL PAIN

In a recent article the usual causes of facial pain are given as tumors or cysts of the mandible, malocclusion of teeth with subsequent temporo-mandibular arthritis (Costen's syndrome), perinasal lesions and sinusitis, an elongated stylomastoid process, and an expanding lesion intracranially pressing on the trigeminal nerve (including tumors of this nerve itself).[1]

In the more classical cases of tic douloureux, no causative factor or agent is ever found. There are many

1. Smith, G. W., *J.A.M.A.*, 166:857-866,1958.

theories on this subject, including arteriosclerosis (an insufficient blood supply to this nerve), pressure on the nerve or its ganglion from surrounding structures, and at a more electrophysiologic level a theory that the pain is reflex in origin and would be likened to an epileptic discharge from the central nervous system.

VARIOUS TREATMENTS ATTEMPTED

The surgeon and the internist have tried their hands at therapy, and as a result a host of drugs have been tried and numerous surgical procedures have been devised and discarded. One author[2] thoroughly covers the medical treatment, past and present, and refers to the use of anticonvulsant drugs such as diphenylhydantoin* in the treatment of this disorder. Since the use of this drug in the treatment of tic douloureux has been evaluated by only a few investigators, the purpose of this paper is to gain a more reliable index as to this drug's efficacy in this role.

METHODOLOGY

At the time of writing, 12 unselected and consecutive cases of tic douloureux had been treated with diphenylhydantoin. Some of these patients had been treated medically and others surgically prior to the administration of the drug. The capsule contained 0.1 gram and the total dosage, which varied from 0.2 to 0.6 grams per day, was given in divided doses through the day. No major complications or side effects resulted, but usually these patients did not tolerate the drug as well as would an epileptic. Due to the small number of patients afflicted with tic douloureux seen in private practice, a control placebo group was not used.

RESULTS

Since tic douloureux is a disorder with spontaneous remissions and periods of relative relief, any evaluation of drug therapy is difficult and uncertain. The results must be taken at face value temporarily and eventually be compared with, and added to, the results of other investigators to form a valid conclusion.

Of the 12 patients treated, five were completely relieved of pain in a short time and required no further treatment of any type. Two patients did not get complete relief, but the pain was so diminished that they did not request any other form of therapy. One patient whose tic douloureux was complicated by what was considered cerebral arteriosclerosis was excluded from the series after therapy had been instituted because its effectiveness could not be properly evaluated. Four patients in the series were afforded no relief, and all of these eventually required surgical intervention.

In those patients who manifested complete or partial relief, the drug commenced to take effect in 24 to 48 hours. In several patients the drug was stopped after the pain had been relieved and the pain did not recur. The anatomical division of the trigeminal nerve which was painfully involved with tic douloureux in no way altered the results of therapy.

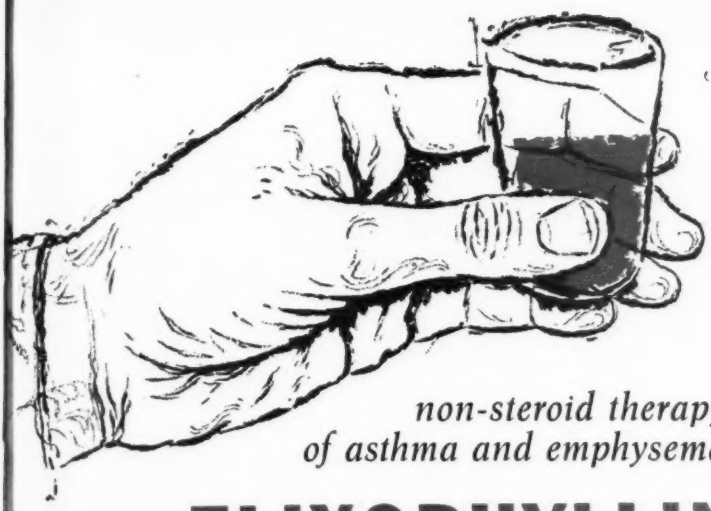
None of the patients developed skin rash, although two became mildly ataxic while taking this drug.

DISCUSSION

There are approximately six published reports concerning this treat-

*Dilantin,® Parke, Davis & Company, Detroit 32.

2. Wartenberg, R., Neuritis, Sensory Neuritis, Neuralgia, Oxford University Press, N. Y., 1958.



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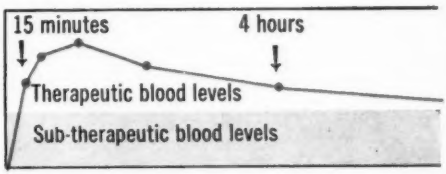

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TABLE I

COMPARISON OF RESULTS OF TIC DOULOUREUX TREATMENT WITH DIPHENYLHYDANTOIN

Investigator	Complete Relief	Moderate Relief	No Relief	Toxic Reaction	Cases Excluded for Various Reasons	Total
Winiker-Blanck[1]	15	7	2	2	1	27
Ende[2]	9					9
Iannone, Baker, Morrell[3]	3		1			4
Dorsey, Hayslip, Anderson	5	2	4	2	1	12
Totals	32	9	7	4	2	52

1. Winiker-Blanck, E., *Deutsche Stomatologie*, 5:321,1955.
2. Ende, M., *Virginia M. Month.*, 84:358,1957.
3. Iannone, A., et al., *Neurology*, 8:126,1958.

ment of tic douloureux. Table 1 compares results of the cases treated by the authors with those treated by others. According to this table, approximately 50 per cent of the patients are satisfactorily relieved of their pain by this medication.

The mechanism of action by Dilantin in ameliorating tic douloureux is not known; however, a theory has been suggested.[3] The original clinical application of this therapy in treating tic douloureux was reported in 1950.[4]

SUMMARY

Diphenylhydantoin, for many years used as an antiepileptic, has recently been used by a small number of investigators in various parts of the world in the treatment of tic douloureux. Although the pain relieving results in this disorder are not startling, the drug shows promise in relieving pain in about one-half of the patients treated.

In this small series, five patients were completely relieved of their pain and two patients were relieved enough to obviate surgery. Four patients were not sufficiently relieved and eventually required surgical intervention.

The data thus far accumulated suggest that this drug merits further investigation, and this may further establish the true value of the drug in the treatment of tic douloureux.

3. Iannone, A., et al., *Neurology*, 8:126,1958.
4. D'Aulnay, J., *These de Bordeaux*, 1950.

Relationship Between Bronchiolitis and Childhood Asthma

Of 100 children aged 4 weeks to 4 years, admitted to hospital with bronchitis, 32 developed bronchial asthma, and 17 developed upper respiratory disorders, perennial rhinitis, or pollinosis. Diagnosis of asthma in 32 children was made between 1½ and 2½ years after original acute bronchiolitis. In only 83 of the 100 patients was reliable family history obtainable. Of these 37 showed evidence of asthma, pollinosis, or eczema.

Wittig, H. J., & Glaser, J., *J. Allergy*, 30:19-23,1959

ORIGINAL ARTICLE

Palliative Treatment of Cancer of the Colon and Rectum

Some suggestions are made for the care of the patient with cancer of the colon and rectum

MAUS W. STEARNS, JR., M.D.,* *New York, New York*

This review concerns the management of the patient who because of locally irremovable disease or nonresectable distant metastases, is considered beyond the hope of cure. This interpretation by-passes several controversial subjects of discussion and allows us to concentrate on the problems encountered in well over half of all patients with cancer of the colon or rectum.

PATIENT STUDY BEFORE MAKING DECISION

Every possible means of determining whether a patient is beyond the possibility of cure must have been exhausted before limiting therapy to palliation. A number of patients each year who have been considered incurable are salvaged because someone was willing to make a last effort to cure.

*Associate Attending Surgeon Rectum and Colon Service Memorial Center for Cancer and Allied Diseases, New York.

OBJECTIVES OF PALLIATIVE TREATMENT

The purposes of palliative management of cancer patients are to relieve symptoms, physical and mental, and perhaps to prolong life in comfort. These purposes differ so from our usual attitudes predicated on our concepts of curing patients, particularly as surgeons, that they demand a fundamentally different approach.

The most frequent and distressing symptoms these patients present are:

1. Pain—resulting from the primary tumor, its recurrence or metastases.
2. Obstruction— intestinal, urinary or biliary.
3. Symptoms resulting from dirty, foul, ulcerating tumor tissue.

PAIN IN THE PELVIS

This pain, with or without radiation down one or both legs, is the earliest and often the only symptom of recurrent tumor following abdominoperineal resection for rectal cancer. In females, if the vagina was not removed at the time of original surgery, digital examination will usually confirm recurrent disease in the pelvis. In males, however, digital examination is not very helpful except in the occasional patient where the recurrence is so located that it can be felt through the perineal scar. Roentgenograms of the pelvis seldom show bone invasion or destruction, even though the recurrence may be massive. Thus in males the history bears the greatest emphasis in making the diagnosis. Usually there is a pain-free period after resection, followed by pain, starting as a dull discomfort which may be attributed to osteoarthritis. Often this is completely relieved by a salicylate taken at regular intervals.

SURGICAL REMOVAL

Surgical excision of these pelvic recurrences following abdominoperineal resection in the male is usually impossible. Surgery has been of some value in cases of recurrence of cancer only in the perineal scar—an unusual occurrence. A few have had two or three years of comparative freedom from pain.

Surgical extirpation may be somewhat more successful in the female. If by digital examination there seems to be the slightest hope of surgical excision, the patient should be given the benefit of the doubt and an exploratory operation done.

IRIDIUM BY IMPLANTATION

More patients are explored since the introduction of local implanted iridium. Iridium is a low-intensity radioactive substance which has a long half-life. A method for the placement of these seeds has been developed which is much more accurate than the older methods of implanting radon seeds. It is still too early for critical evaluation, but it seems that localized recurrence, accessible for implantation, is more satisfactorily treated in this manner than by external radiation.

HIGH-VOLTAGE X-RAY

If surgical excision or implantation with radioactive iridium is not possible, high-voltage x-ray therapy seems to offer more chance of pain relief than any other agent when the pain has progressed so that it can no longer be controlled by salicylates. This should not be given in doses that are considered curative. The lack of enthusiasm for the use of x-rays in the management of bowel cancer is attributable to its failure as a curative agent. Some radiotherapists consider the attempt relieve symptoms with less than accepted dosage as somewhat akin to quackery. The usual treatment suggested is 400-500 r in air through each of four or six large pelvic portals, treating one portal daily or two portals every other day. Frequently this will relieve pain for periods of up to six months. When the pain recurs, another cycle is given. If the initial course of x-ray therapy

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gives no relief it is usually of no avail to give additional x-ray.

TIME TO REFER TO NEUROSURGEON

If no relief is obtained with x-ray therapy the patient should be referred to the neurosurgeon. Most neurosurgeons are not enthusiastic about chordotomy because of the incontinence and paralysis that may follow, as well as the occasional indifferent result. The patients do not risk the procedure unless their pain is unendurable. If the patient refuses chordotomy and the pain is confined to the pelvis, alcohol nerve block may be used and occasionally it is very effective.

WHEN TO GIVE MORE POWERFUL ANALGESICS

Some time before this stage has been reached some narcotic is required, in addition to salicylates. Only in the terminal phases is anything stronger than codeine in combination with aspirin necessary. This combination is more effective for a longer time than any other narcotic. Aspirin should be given at regular intervals rather than only when the patient is aware of pain. Codeine is added when the aspirin alone is no longer effective.

EXPERIMENTAL CHEMOTHERAPY

When these means have been exhausted, and if the patient or his family request it, the experimental chemotherapeutic drugs are used. Any one of them may be temporarily useful.

PAIN OF RECURRENCE

Pain associated with recurrence following anterior resection is handled in a similar manner. However, diagnosis is usually made earlier when proctosigmoidoscopies are part of the routine postoperative follow-up, and attempts at surgical excision or implantation with iridium are more often feasible.

INTRA-ABDOMINAL PAIN AFTER RESECTION FOR COLON CARCINOMA

This pain is most frequently due to intestinal obstruction of varying degree or pressure by a mass. Those cases without obstruction are difficult to evaluate, and usually, if the general condition is reasonably good, require surgical exploration for determination of further treatment. Sometimes a mesenteric or omental mass can be excised that has caused pain by its mere weight, or an inoperable recurrence can be implanted with iridium seeds. If the recurrence is too extensive for implantation, its borders can be outlined by silver clips so that external radiation can be directed more accurately.

LIVER PAIN

Pain in the liver is not infrequently caused by liver metastases. Implantation with iridium offers little. X-ray therapy in low dosage, from a high-voltage unit, seems the most effective agent in relieving this pain.

INTESTINAL OBSTRUCTION

This condition may be complete or partial, intra-abdominal or intra-pelvic. The former type may involve the small or large bowel. Many patients tolerate the incomplete obstruction of cancer with a minimum of discomfort, using mild laxatives regularly. A syndrome of pain in the mid-abdomen with backache, is not infrequently seen with partial small bowel obstruction. The diagnosis of obstruction is confirmed by roentgenograms. The high obstructions

cause early vomiting, give a short history of pain, and x-rays show very little distention of the bowel. High obstructions require operation within a day or two. When the obstruction is lower or in the large bowel conservative efforts may be used. These consist of the use of mineral oil and/or milk of magnesia in small amounts through a long intestinal tube passed into the small bowel.

WHEN TO EXPLORE

If conservative efforts prove unavailing, exploration is usually indicated even though there is palpable recurrent tumor. Some neoplastic adhesions can be cut, relieving obstruction, but more often some type of by-pass procedure is indicated. When possible, the by-pass procedure should completely divert the fecal stream. If this is not done, and normal channels are left in continuity, cramps will usually continue from the attempt of the bowel to follow normal pathways rather than the artificially-created one. Moreover, because of incomplete diversion, infection may result in the obstructed segment. A complete diversion is usually easily accomplished by anastomosing the proximal distended bowel end-to-side to the distal bowel beyond the obstruction. The distal end of the obstructed bowel is brought out as a mucous fistula. This prevents continued passage of bowel content into the obstructed portion and allows free drainage and irrigation of this loop.

When obstruction due to pelvic recurrence follows either a "pull-through" procedure or an anterior resection, the patient can be treated by conservative means for a considerable length of time before a proximal colostomy has to be done. Often this can be postponed still further by x-ray treatment, as previously described.

RECURRENCES TREATED BY IRIDIUM

A number of anastomotic and pelvic recurrences following anterior resection have been treated by implantation of iridium with temporarily satisfactory results, *i.e.*, regression of the bulk of the tumor, cessation of bleeding, mucosal regeneration over the residual tumor, and cessation of the irritating rectal discharge.

URINARY OBSTRUCTION

If the obstruction occurs early in the postoperative period, it is usually non-neoplastic in origin and, after the site of obstruction has been determined, it should be attacked by nephrostomy, ureterostomy, or ureteral transplant. Such obstruction occuring later in the postoperative period is usually caused by invasion of neoplasm. Good judgment has to be used in deciding the prognosis in terms of symptoms, life expetancy and so on. Usually urinary obstruction is seen when the patient is beginning to go downhill rapidly, with other signs of recurrence. To subject a patient in this condition to bilateral nephrostomies for the possible prolongation of life a few months, while he continues to have other difficulties, hardly constitutes palliation.

X-ray therapy has not proved successful in opening any of these ureteral obstructions. Indeed, probably due to edema, some partial obstructions have been converted to complete obstructions.

BILIARY OBSTRUCTION

This condition, manifested by jaundice, is not infrequent in terminal cancer patients. Occasionally jaundice appears two or three years post-

operatively in a patient who otherwise appears in good condition. The natural tendency is to ascribe this to metastatic cancer and pursue a hands-off course. While the majority will be found to have metastases blocking the biliary tree, sometimes the jaundice will be found to be due to stone or inflammatory pancreatic disease and warrant thorough investigation before writing the patient off as incurable. Usually this involves exploratory laparotomy.

PROBLEMS OF HYGIENE

A group of symptoms result from ulcerated, foul, necrotic tumors appearing either as metastasis or direct invasion of the abdominal wall or pelvis.

The tumors involving the abdominal wall or soft parts are often amenable to surgical excision, the treatment of choice, as it affords promptest palliation and sometimes results in surprisingly long survivals. The lesions which appear on the abdominal wall often look much worse than they behave. They should be excised if possible and the wall and underlying bowel closed as well as possible. The frequently resulting hernias are surprisingly well handled with surgical belts.

The pelvic recurrences that appear in the perineum as ulcerated tumor tissue are not often amenable to surgical excision. X-ray treatment has not accomplished much. Intra-arterial nitrogen mustard has done no more than roentgentherapy, and its effects have been of shorter duration. Locally-implanted iridium seems to offer the most palliation.

In this type of recurrence general hygienic measures are of more value than almost anything else. Pressure sprays, suction, acriflavine, zinc peroxide dressings and deodorizing solutions are of very real value in making a patient's life less uncomfortable, and less offensive to himself and his family.

ASYMPTOMATIC METASTASES

In a number of patients, routine follow-up examinations will disclose metastases that present no symptoms. These create a real question as to management. If the metastasis represents the only known or demonstrable disease, it should be removed surgically where possible. If it is only one of multiple manifestations of recurrence it should be left alone so long as it remains asymptomatic.◀

Treatment of Coryza

A susceptible subject may have a cold lasting three weeks and then catch another after only a few clear days. This type of patient can be improved by giving a small dose of anticatarrhal vaccine every month from the beginning of September until the end of April.

Vaccine treatment should be continued for as long as the patient considers it necessary. The natural history of the disease is that people vary enormously in susceptibility, and the same person varies at different epochs of his life. Children are much more prone to colds than adults, old people much less so. Anticatarrhal vaccine produces good response in children, but a certain amount of parental determination to persevere is required. Of course, there are patients in whom vaccine fails altogether, others who get two colds in a winter instead of eight. If selected intelligently, 50 to 75 per cent of patients benefit.

Moor, F., *Brit. M.J.*, 1:789-790,1959.

CLINICAL NOTE

A New Anti-Infective Solution in the Treatment of Acne

This preparation was found to be especially effective in the subacute pustular phase of acne

SALVATORE J. MESSINA, M.D., *Boston, Massachusetts*

Acne vulgaris is most commonly seen in adolescents and young adults. It occurs so frequently that many have considered it a normal varient and have permitted delays in therapy, reassuring the patient that the lesions will disappear and no great harm accrue.

That this is not true is borne out by the existence of numerous shattered personalities severely affected by the psychological handicap of this disfigurement in adolescence, when self-esteem is sorely needed.

For this reason treatment is best instituted as soon as the lesions are discovered. If not, they advance with increasing severity and enhance the risk of permanent disfigurement.

EARLY SYMPTOMS

The earliest manifestations of acne vulgaris occur in the pre-adolescent period, with comedones on the chin, nose, and forehead. At this time, the skin is oily. Later the lesions are papules and pustules, and at this time spontaneous recovery may take place. When pustules are numerous, the disease is predominantly secondarily infected. In the severe cases there is extreme involvement not only of the face, but of the chest, buttocks, arms, and even the axillae and groins.

ETIOLOGY

The many factors associated with acne include:

1. *Diet.* Exacerbation of the disease may follow ingestion of certain foods.

2. *Seborrhea.* This is first seen at puberty, indicating a relationship with increased endocrine activity. Premenstrual flare-up is common. Hormonal influences on acne have been previously cited.[1,3]

3. *Infections.* Bacteria invading the sebaceous glands play an important role in the formation of pustules.[4,5,12] These lesions often give rise to deep pitting and scarring leading to permanent disfigurement.

4. *Miscellaneous.* This includes worry, lack of sleep, constipation, ingestion of iodides and bromides, and exposure to oils, greases, and waxes.[6]

TREATMENT

1. Diet.[7]

2. Local measures including expression and drainage of the pustules.

3. Control of seborrhea.

4. Estrogens used judiciously in females over age 18 and rarely in males with severe disease. Topically applied, estrogens also have a definite use.[8,9,10]

5. Vitamin A also plays a part in the process of keratinization and is of value in the type of acne characterized by numerous comedones, small cysts, follicular papules and milialike lesions.[11]

6. Ultraviolet irradiation usually improves the patient.

7. X-ray therapy is reserved for the patient in whom other therapies have failed.

In the infectious stage of acne, the lesions are predominantly pustular. If the pustular phase is acute, courses of therapy with the broad spectrum antibiotics may be indicated. In the less acute cases, the use of a preparation containing hexachlorophene in cetyl alcohol and isopropyl alcohol* effectively replaces the wet dressings of boric acid and Burow's Solution often used.

The isopropyl alcohol acts as a bactericidal agent on contact and on evaporation leaves an odorless invisible residue of hexachlorophene bound to the skin by an invisible layer of cetyl alcohol for prolonged bacteriostasis. This preparation meets the criteria suggested by Sulzberger and Baer[13] as an agent for external use against infections of the skin. Their criteria are:

1. High efficiency.

2. Low allergenic potential.

3. Very low local primary irritancy.

4. Low incidence of neoplastic change after long continued use.

5. Low systemic toxicity by absorption.

6. Ease of incorporation and stability in suitable vehicles.

7. Acceptance to users (little messiness, stinging, odor or staining).

STUDY

Twenty-five patients, 10 males and 15 females, aged 11 to 32, who manifested pustular acne lesions and

1. Hamilton, J. D., *J. Clin. Endocrin.*, 1:5703,1941.
2. Geecherman, W. H., *Arch. Dermat. & Syph.*, 61: 237-243,1950.
3. Way, S. C., & Andrews, G. C., *Arch. Dermat. & Syph.*, 61:575-588,1950.
4. Evans, C. A., et al., *J. Invest. Dermat.*, 35:305-324,1950.
5. Macdonald, T. C., & Taylor, F., *Lancet*, 2:558-561,1951.
6. Schwartz, L., & Peck, S. M., *New York J. Med.*, 43:1711-1718,1943.
7. Flood, J. M., *Pennsylvania M.J.*, 51:533-535,1948.
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10. Philip, A. G., *New York J. Med.*, 51:1313-1314, 1951.
11. Davidson, D. N., Sobel, A. E., *J. Invest. Dermat.*, 12:221-228,1949.
12. King, W. C., & Forbes, M. A., Jr., Current Therapy, 1959. W. B. Saunders Co., Philadelphia, Pa., 419,1959.

*Pro-Blem®, Hoyt Pharmaceutical Corporation, Newton 58, Massachusetts.

13. Sulzberger, M. D., & Baer, R. L., *1949 Year Book of Dermatology and Syphilology*, The Year Book Publishers, Inc., Chicago, p. 10, 1950.

whose response to the usual therapy was not satisfactory were selected. All were treated with various other agents, but in addition were told to apply the hexachlorophene and alcohol preparation with a cotton pledget to the involved areas at least 4 times daily for three to six weeks. Improvement was based on less inflammation, fewer pustules, and more rapid drying up of lesions.

Of the 25, 20 (80%) showed definite improvement of the inflammatory pustular stage of acne. Decrease in skin oiliness also was noted. The older patients with more inflammation and considerable seborrhea showed the greatest improvement. The remaining 5 (20%) manifested no improvement or significant change. One patient claimed a dryness effect from the medication which she considered excessive and one patient reported a stinging sensation of brief duration following application. The preparation is clear and unnoticed on the skin, a factor in its cosmetic acceptance for daytime use.◀

Care of the Urinary Bladder After Operation

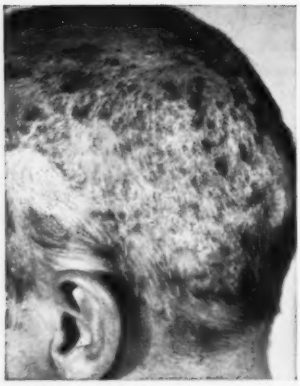
Following operation the bladder must be emptied three or four times daily to avoid stretching. Fluids given intravenously accumulate rapidly in the bladder, yet often a liter or more is ordered immediately after operation. The house staff and nurses should be cautioned against catheterization unless absolutely unavoidable. Infection follows catheterization. Some patients will dribble painlessly from a full bladder instead of complaining of distention.

Dodges used to evoke urination should be used only until distention becomes mildly uncomfortable. The gentle, aseptic passage of a small, well lubricated catheter does no harm unless the bladder has been damaged. If it has to be repeated more than once or twice, a Foley-Alcock catheter should be left in and connected through one arm of a sterile glass Y-tube and rubber tubing to a sterile reservoir, hung at the bedside and containing sterile water or a mild antiseptic, the other arm going to a sterile empty bottle beneath the bed. The value of prophylactic antibiotics while a catheter is being used is debatable.

Because of the frequency of postoperative urinary retention, it seems wise to insert a Foley catheter at the start of an extensive operation to be left in place until the patient is able to move about freely. After its removel, if he voids frequently with straining or has retention a Foley catheter is used to measure the residual urine and is left in place if residual urine exceeds 75 to 100 cc.

If a patient who has had urinary difficulty prior to operation requires recatheterization his condition may improve with pilocarpine or urecholine. If residual urine or retention resists these measures, cystoscopic examination is indicated. In cases of retention due to injury of the spinal cord, if the Crede maneuver fails or is impracticable, an inlying catheter with an irrigator should be used. If innervation of the bladder is permanently destroyed, cystostomy should be done.

Creevy, C. D., *Northwest Med.*, 57:1589-1591,1958.



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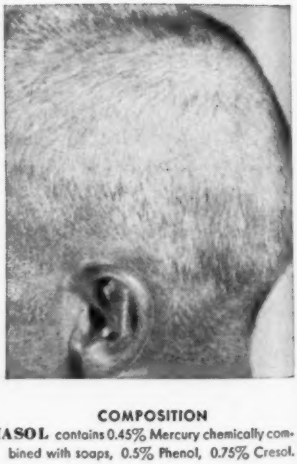

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Investigations in a Case of Murder by Insulin Poisoning

A case is presented in which insulin was recovered from a body five days post-mortem

V. J. BIRKINSHAW, F.P.S., *London, England*

A woman of 30 returned home from her work in a laundry for her midday meal. At 11:20 p.m. on the same day she was found dead in the bath, which was empty when the police arrived.

The body, which was left undisturbed until seen by the pathologist at 3:30 the next morning, lay on its right side in the empty bath. The hands lay in front of and slightly below the face; the fingers of the right hand were loosely curled round the left wrist and the left hand was in a position of natural sleep. Blood-stained froth ran from the nose; the pupils were widely dilated. Fragments of vomited food were in the hair and on the sides and bottom of the bath. Caught in the crook of the right elbow were 110 ml. of clean water. The skin was damp where it came in contact with the surface of the bath, the bottom of which was also damp. Rigor mortis was developing, the face was cyanosed and there was hypostasis on the right side of the body. There were no obvious signs of violence, and the only other things in the bath were a wet face-cloth, soap and a soapdish.

The police noted the walls of the bathroom were dry and there was no splashing on the floor. In the hand-

basin were two pillow-cases soaking in water and stained with vomit. In the main bedroom were some lady's sweat-soaked pajamas, and a man's dressing-gown and pajamas which were quite dry. One side of the double bed was disturbed as though someone had slept on it. In the kitchen were found a pair of vomit-stained sheets, in a washtub, two hypodermic syringes, one wet, four needles, and many drugs, including quinine. No insulin or insulin vials were discovered.

The history from the husband was that after her midday meal the woman had done some housework and washing, at 5 p.m. she had toast, grapefruit, bread, butter and tea with sugar, and then retired at 6 or 6:30 p.m. At 7:30 p.m. she had asked to be called so that she could watch a television program but she felt "too comfortable to move" and remained in bed. At 8 p.m. she was "too tired" to say good night to her stepson. At 9:20 p.m. she called to her husband, who came upstairs and found that she had vomited on the bed. Having changed the bedclothes, he retired. His wife, who complained that she was "feeling too warm", lay on the bed. Later she removed her pajamas in the bedroom and went to have a bath while her husband remained in the bedroom reading. He dozed off and when he awoke at 11:20 p.m. his wife had not returned. He found her submerged in the bath and apparently drowned, so he removed the plug to let the water out. As he was unable to lift her from the bath and his efforts at artificial respiration were unsuccessful, he then summoned assistance. The husband also said that his wife was pregnant.

The suggested immediate cause of death had been drowning, confirmed at post-mortem. Specimens were taken for chemical analysis, but no common poisons or abortifacients were found. Heart blood to which no preservative had been added showed glucose 210 mg./100 ml. seven hours later.

It was difficult to explain why a healthy young woman should have drowned in her bath without any apparent signs of reaction to inhaled water; she lay as though asleep with no evidence of splashing or violence. It was concluded that immediately prior to her death she had been unconscious and that the agent responsible for this had made her sweat and vomit and dilated the pupils—all suggesting that the woman may have been hypoglycemic. The glucose concentration in the blood appeared to contradict this hypothesis, but this has little value as an indication of the glucose level in the blood during life.

Five days post-mortem the body which had lain on a mortuary slab at room temperature in mild weather conditions was again examined, and under better lighting four hypodermic injection marks were found, two in each buttock. The tissues underlying were excised and found to contain insulin, 84 units in 170 gm. of tissue. These findings and control experiments indicated that at the time of death the buttock tissues had contained at least 240 units of insulin, a dose sufficient to produce either the soporific or comatose stages of the hypoglycemic state. No insulin was found in washings from the wet hypodermic syringe or needles.

Two months later the husband, a trained male nurse, was arrested and charged with the murder of his wife.

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dle-aged man had intermittent low back pain that he attributed to injuries received in an automobile nt three years previously. The pain radiated down both legs, making the patient walk bent over. He also ficulty getting out of bed and had to pull his knees up and roll out. Any heavy lifting precipitated a ack, and he tired easily.

gs on x-ray of the thoracic and lumbar spine gave negative results. Findings from other laboratory were within normal limits. A herniated disc, although still a possibility, was temporarily ruled out neurologic examination. Previous treatment consisted of analgesics and steroids (without success), and s were given during severe attacks.

ing a dosage of Trancopal, 100 mg., three times a day, this patient is able to walk almost normally and n his regular activities as long as he does not overexercise. He has been taking Trancopal over seven with excellent relief of symptoms. No side effects have occurred. *Clinical Report on file at the Department of Medical Research, Winthrop Laboratories.*

INDICATIONS: Musculoskeletal: Low back pain (lumbago, sacroiliac pain); neck pain (torticollis, etc.); bursitis; rheumatoid arthritis; osteoarthritis; disc syndrome; fibrositis; ankle sprain; tennis elbow; myositis; postoperative muscle spasm.

Psychogenic: Anxiety and tension states; dysmenorrhea; premenstrual tension; asthma; angina pectoris; alcoholism.

Dosage: 100 to 200 mg. orally three or four times daily. Relief of symptoms occurs in fifteen to thirty minutes and lasts from four to six hours.

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He denied having injected insulin, but explained the presence of the injection marks by stating that on several occasions he had injected his wife with ergometrine maleate in therapeutic doses during the two weeks preceding her death in an attempt to procure abortion. He said he gave the last injection after the midday meal on the day of her death. The actions of this drug do not explain the signs and symptoms found in this case, and analysis of the urine and part of the buttock tissues did not reveal its presence.

The accused man was found guilty and sentenced to life imprisonment.

The experience gained in these investigations enables certain observations which might prove useful should a similar problem arise in the future. The necessity for early attention to minute details in postmortem examination is well emphasized by this case. The fact that the body was not disturbed after it was found resulted in the water being discovered in the crook of the elbow, and this significant finding threw considerable doubt on the accused man's claim that he had attempted artificial respiration. The injection marks on the buttocks were missed during the first examination because of the unsuitable quality of the mortuary lighting. The difficulty in assessing what material should be retained for histological examination requires careful consideration in cases of sudden death. In this case material from eight major organs was preserved, but the pancreas, pituitary, and suprarenal glands were not examined microscopically. Adequate samples, were, however, taken for the toxicological analysis, which followed a comprehensive routine. All common poisons and drugs were thus excluded at an early stage, and the absence of ergometrine in the viscera was established long before its use was alleged by the accused man.

The vomiting, sweating, and gross dilation of the pupils observed in this case are not specific signs of hypoglycemia. More objective evidence would have been desirable, and in other cases might prove essential. As to the changes which occur in the glucose level of the blood after death, glycosis occurs more slowly in the cerebrospinal fluid after death, and the glucose level in such a specimen taken after death gives a better indication of the blood-glucose concentration during life. It is, however, difficult to obtain a sample of cerebrospinal fluid uncontaminated with blood. In cases of suspected hypoglycemia, blood should be drawn from the left side of the heart within two hours of death; this is not always practicable. In all cases of sudden death the most useful information can be obtained by analysis of a specimen of peripheral blood from the femoral vessels and preserved with fluoride. Such a specimen cannot be used for blood grouping. The glucose content can be estimated and the result might be of some use in the assessment of the ante-mortem level. In addition it can be analysed for poisons and drugs, including alcohol. Somewhat surprisingly the subject of post-mortem blood-sugar levels is not referred to in many of the current standard textbooks on forensic medicine.

In the present case the possibility had to be considered that hypoglycemia might have been due to natural causes. The fact that the deceased was a healthy young pregnant

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woman ruled out most of the possible causes of spontaneous hypoglycemia, but there remained the possibility that an islet-cell tumor could have been responsible. Such tumors are often very small and might easily be missed during routine post-mortem examination. In this case the large amount of insulin recovered from the buttock tissues and its uneven distribution excluded the possibility of endogenous secretion.

The possibility that the woman's condition was due to ergometrine injections administered by the husband was excluded on several grounds. No ergometrine was found in the urine, the buttock tissues, or the viscera, and it was also shown that ergometrine does not exert effects in mice or on rat diaphragm such as those produced by the tissue extracts from the deceased woman. In addition the clinical effects of ergometrine are known to be short-lived; its action starts in a matter of minutes and its effects pass off within an hour or two.

The successful extraction of insulin from tissues obtained from the body five days after death seems surprising. Insulin is, however, stable in acid media, and lactic acid is released after death in peripheral muscular tissue. Insulin injected into human tissue cannot be recovered if the tissue is first allowed to putrefy, and for this reason it is essential to obtain tissue samples before putrefaction begins and to store them without addition of preservative at 0°C. until they are extracted. There is no available chemical or physico-chemical method for the detection and identification of insulin in crude protein extracts. Its biological activity has to be detected and compared with that of the hormone itself. With the rat-diaphragm technique it is possible to detect less than 1 mili-unit.◀

Brit. M.J., 2:463-468,1958.

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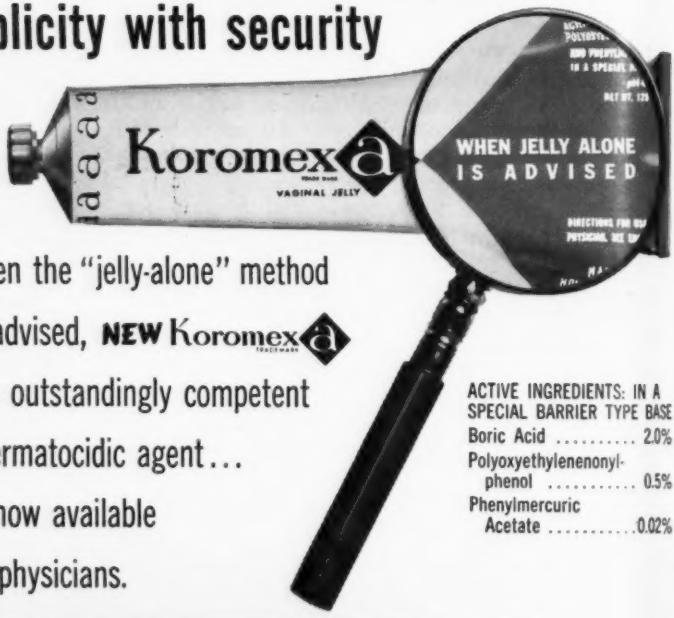

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The Peristaltic Enema

The two-way peristaltic enema was used in the treatment of 35 constipated patients, with excellent response

ROBERT E. MULLARKY, M.D., *Seattle, Washington*

Giving the peristaltic enema is a very simple procedure using simple apparatus. The "tube" is a combined ⅛ inch and a ⅜ inch rubber tube built up into a single tube 6 inches long, which then divides into the original two tubes, which are connected to the reservoirs. The smaller tube is open ½ inch from the oval tip, while the large tube has two ½ by ¼ inch openings, ⅝ and 2 inches back from the tip.

The small inflow tube allows for injection of solution into the rectum; the rate of flow is, however, mainly controlled by pressure in the lumen of the bowel itself. The outflow tube with its two large openings allows free backflow, thus preventing cramps and premature evacuation contractions.

The inflow and outflow tubes are each connected to a 2 ounce hand-bulb, which is in turn attached to the apparatus. The bulb connected to the small tube is for slight rhythmic stimulation to the rectum, thereby initiating peristalsis of the colon when desired and keeping the tube free of feces. The other bulb is used to clear the backflow tube if it becomes blocked by feces.

There are two one-quart reservoirs attached to a stand with a foot that slips under the mattress, one of which is connected to the inflow tube, the other two inches lower to the outflow tube. The reservoirs can be elevated

one to 24 inches above the mattress, but are always kept at the level of the crest of the ilium while in operation. As the solution slowly trickles into the rectum, the peristaltic rhythm of the bowel causes an ebb and flow through the larger outflow tube and into the outflow reservoir. A third tube is connected to the base of the outflow can and to a waste bucket on the floor for rejected solution containing feces, to be discarded, and an equal amount of clean solution added to the supply can.

The nurse pours eight ounces of solution at 105° F. into the supply can, inserts the rectal tube exactly four inches, and then opens the valve allowing the solution to flow into the rectum. Thereafter the solution automatically flows back and forth between patient and apparatus with rhythmical ebb and flow, in time with the peristalsis of the rectum and colon. With each inspiration the solution is drawn further up in the colon. The continuous but very low pressure causes the solution to run quickly to the cecum through a relaxed bowel without producing cramps. Fecal masses slow the flow of solution, but very little. The peristalsis becomes stronger, up to defecation urge, usually in about one hour.

If the bowel is very sluggish, from eight to 16 ounces more fluid may be added, or the rectum may be stimulated by manipulating the inflow bulb. When the patient is ill or the bowel is distended the amount of solution should never exceed eight to 10 ounces. At the end of the soaking period a defecation contraction may be produced by elevating the reservoirs and thus suddenly injecting the solution remaining in the inflow and outflow tubes.

The introduction of two ounces of ice-water into the rectum will cause an immediate and powerful evacuation contraction of the colon. Enema solutions at 105° F. are very effective in relaxing spasm of the bladder neck and relieving postoperative urinary retention.

The peristaltic enema is an excellent means of introducing medication into the colon, to be retained as long as desired. Solutions of acriflavine, amebicides, sulfa drugs or antibiotics may be effectively administered by this method. The entire colon and even the terminal ileum can be painlessly and effectively bathed with a non-irritating solution for long periods.

When used to carry in surface active agents, it is most effective in softening impactions due to barium, psyllium seeds or bran, and masses of bulk laxatives. The effect of fecal impaction softeners is enhanced and prolonged by adding methylcellulose to the solution. Normal defecation occurs in 45 to 60 minutes.

The peristaltic enema should always be used when the patient is seriously ill or is distended and a "return flow" enema is indicated, especially after abdominal surgery where strain on a suture line must be avoided. It is specifically indicated in paralytic ileus from any cause and in all cases of fecal impaction in the upper colon. It frequently obviates the necessity for a 2-stage bowel resection, because by its use the bowel can be emptied after all other methods fail.

Patients under sedation with an opium derivative have a "paralyzed" bowel and must have an enema every day or two. Radiotherapy over the abdomen causes less nausea if the colon is clean. Soapsuds enemas or laxatives produce irritation and con-

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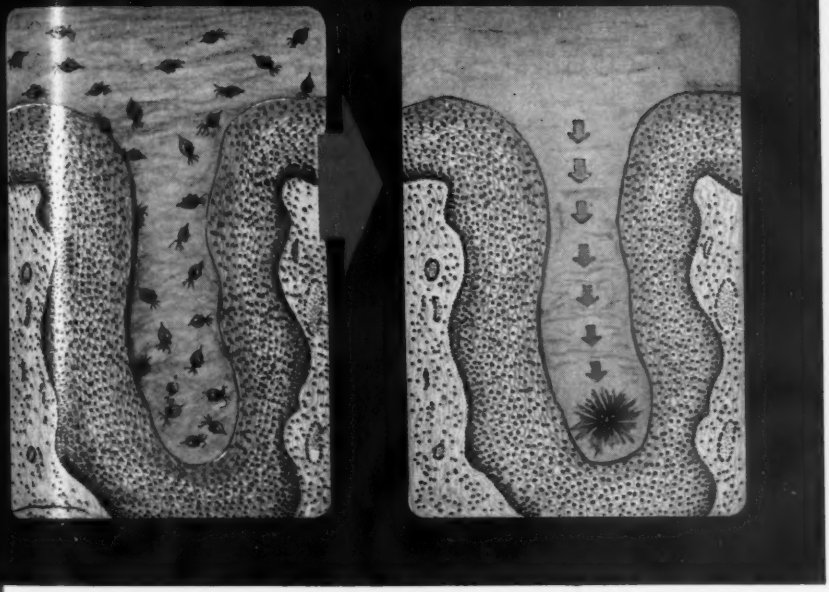

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gestion of the bowel with resulting increased radiosensitivity. A peristaltic enema before radiation will empty the colon without irritation and results in a more comfortable post-radiation course.

Studies of use of the peristaltic "2-way" enema made on 35 constipated but otherwise normal adults, with bowel pressure readings and survey x-ray films of abdomen, showed that small amounts of isotonic sodium chloride solution quickly reach and enter the terminal ileum without producing discomfort, soften and liquefy fecal masses in the colon and induce a normal defecation reaction. Such an enema is indicated in all seriously ill patients with constipation, ileus, or low-bowel obstruction. It is an excellent way to empty the colon before gastrointestinal surgery, and before abdominal therapeutic or diagnostic radiation. It is a useful therapy for diseases of the colon by medicated solutions, because it completely bathes the mucous membrane of the bowel for long periods, without causing cramps or distress. It is valuable for fecal impactions or a loaded colon in patients with transverse myelitis, multiple sclerosis, or megacolon. It is useful in any case of obstipation and invaluable, even life-saving, in many "problem" cases such as a blocked colostomy, an enema that "will not return" or a patient under opiates or in a body cast.◀

Northwest Med., 58:209-218,1959.

Abnormal Uterine Bleeding

The newer hormone preparations have made it possible to check certain types of abnormal menstrual flow almost without regard as to etiology. Too often a malignant tumor, an accident of early pregnancy or even infection may be overlooked in the haste to stop the hemorrhage by an injection or by oral therapy. The woman may come to biopsy or curettage or both after an unnecessary or even tragic delay. There is still no substitute for an adequate examination and a firm diagnosis as the basis for treatment.

Irradiation therapy should be considered only for patients at or during the menopause and, even so, the popularity of this mode of therapy of abnormal uterine bleeding has diminished in recent years.

The cause of abnormal uterine bleeding can be removed in almost every case if a determined effort is made. No method exceeds surgical dilation and curettage for diagnosis or therapy. The "medical" curettage does not suffice in the case of the elusive cervical or uterine polyp, certainly not in that of the submucous fibroid. Suction curettage, although revealing in many cases, is not a therapeutic measure. Although cervical and vaginal smears will do much to disclose a cervical cancer, the accuracy of the cytologic diagnosis of uterine cancer still leaves much to be desired.

Once a firm diagnosis is made, especially in cases where anovulation is the basis of abnormal bleeding, the use of the newer potent hormones is logical. Individualization will be necessary in each case.

Benson, R. C., *Northwest Med.*, 58:31-34,1959.

Hereditary Aspects of Disease

The significance of genetic influences on human variability are only beginning to be understood

BARTON CHILDS, M.D., *Baltimore, Maryland*

GENETICS-GENES

Genetics is the study of heritable variation. The genetic constitution possessed by an individual provides him with a long list of potentialities, which are or are not realized, depending upon the kinds of environment in which it is called upon to function. A particular variation, whether it be disease or not, is caused by a particular gene operating in a favorable environment, and a change in either component will alter it. For example, a person who does not possess the gene causing galactosemia will not have that disease, but equally such a gene would probably remain one of the secrets of nature in a society which did not use milk. This point is stressed at the outset because, to ameliorate genetically-determined disease, the physician must so alter the metabolic environment as to render the effects of the deleterious gene harmless, and in order to know whether or not this is possible he must know how the gene acts.

CHROMOSOMES

Our gnowledge of genes is not precise. We can detect the presence of a gene only when it exists in two or more alternative forms reflecting themselves as two or more variants of a characteristic in a population, and segregating in families according to Mendelian laws. We know also that in

the chromosomes, in which the genetic material resides, each gene occupies an allotted locus. A sexually reproducing organism will have in each cell two homologous chromosome sets, and the homologous loci in these chromosomes may be occupied by two representatives of the genetic material which are identical, or by two which differ from the other. If identical, we say the cell and individual are homozygous; if different, heterozygous. It is possible for genes occupying homologous loci to be different because of mutation; presumably a change in the genetic material has occurred during replication. Such a change is then reflected in some alteration in the metabolism of the cell, creating therby a new variant of a particular characteristic, a new phenotype. From this it may be infered that though a given locus may be occupied by different genes, all the genes at that locus are concerned with the same function; thus a gene may be defined as a unit of mutation and a unit of function. During the formation of the germ cells, the homologous chromosomes intertwine and parts of each may cross over and interchange with the other, so that what segregates into the zygote is a unique chromosome with new combinations of genes. Since the points of breakage and crossing over appear to be random, a gene may be defined as the smallest unit of the genetic material which cannot be broken by crossing over. The most recent evidence suggests that those three units are not the same, but that a larger functional unit contains many smaller units of mutation and of crossing over.

HOW METABOLISM IS REGULATED

It is apparent that genetic control of cellular metabolism is mediated by the influence of the genetic material upon the contruction of proteins; it seems likely that each gene locus bears a functional relationship to some protein molecule. Whether the affinity between gene and protein is a direct one, or is achieved in some indirect way, each gene has a single function, and that function is mediated by a protein. Enzymes are proteins and have as their function the control over reaction rates. Thus, we may make a final definition of genes as units of the genetic material which control the specificity of the cell proteins, and ultimately the balance of metabolic reaction rates.

GENETIC VARIANTS AND DISEASE

What of the genetic variants and disease which confront the physician? It is reasonable to assume that every gene operates in the way just described, whether its ultimate phenotypic effect is a morphological variation, a defect in renal tubular reabsorption, or an abnormal hemoglobin. Most commonly, genetic etiology is suggested by familial aggregations of persons showing some obvious variation, and we speak of gene action only in terms of a description of the characteristic itself. Antigen specificity is a reflection of structure and configuration and is related to gene specificity. Genes occupying at least one locus concerned with hemoglobin formation may be distinguished by variations in electrophoretic mobility and solubility; and the relationship of genes to protein structure has been brilliantly demonstrated.

Enzyme systems lend themselves to assessment. Normal enzyme may be present in normal concentration, but be inhibited; or the concentrations of

substrates or cofactors, themselves sometimes under genetic control, may be reduced. Indeed, it may be difficult to assign primary responsibility for reaction failure to the appropriate gene.

A CELL THE SITE OF MANY REACTIONS

The living cell must be considered as a multiphase system in a dynamic state in which reactions are coupled, sequential, or otherwise interdependent so that reaction failure at one point must lead to alteration of reaction rates elsewhere. Early geneticists were principally concerned with morphological variations, and gene action was related directly to the characteristic being studied. Any rapidly developing discipline has its own semantics.

SOME TERMS AND THEIR MEANING

Chief among these is dominance. A fully dominant gene is one which expresses itself equally well as both heterozygote and homozygote, and a recessive gene is one which expresses itself only in the homozygous state. When we consider conditions amenable to biochemical examination, we see that our description of gene action depends upon what measurements we make. There is perhaps no better example than that given by the genes at the hemoglobin locus. If we consider sickle-cell *disease* alone, the distribution of this characteristic in families suggests a recessive gene; i.e., all affected will usually appear in one generation. If we consider sickle-cell *trait* alone, the distribution is that of a dominant gene, while consideration of *both* trait and disease together suggests a gene showing incomplete dominance. Hemoglobin electrophoressis reveals no dominance; in the heterozygote the product of both genes, hemoglobins A and S, are present together.

A POPULAR PASTIME

Hunting for heterozygous expressions of recessive genes is a popular pasttime just now. We have recently been dealing with some families containing patients with familial nonhemolytic jaundiice. The distribution of cases in familiies suggests segregation of a recessive gene, and there is evidence that the defect in such patients is one of making an excretable glucuronic acid conjugate of bilirubin. Because of this, bilirubin accumulates and the patient is always jaundiced. Parents and sibs, however, are neither jaundiced, nor show any hyperbilirubinemia. Our studies showed that parents, some sibs, and some grandparents exhibited a capacity to manufacture glucuronic acid conjugates of the test substances, greater than that of the affected patients but less than that of the normal controls. Thus with respect to jaundice this gene is fully recessive, but with respect to glucuronic acid conjugation of test substances, it shows partial dominance.

ANTICIPATIONS AND WHY?

We may look forward to a time when all such recessive genes will be found to exhibit some detectable effect in heterozygotes. A gene whose effect is undetectable is said to be impenetrant, and families are described in which someone marked as the possessor of the gene in the direct line of passage has not shown the characteristic. But like dominance, the penetrance or impenetrance of a gene is determined by success or failure in the detection and measurement of one or other of many parameters. It may be that the gene effect is

detectable only in the presence of some special environmental condition. In certain circumstances a gene may be so impenetrant as to leave us unaware of its existance.

A REMARKABLE HAPPENING AND A SPECULATION THEREON

Among the substances capable of causing hemolysis of susceptible cells are the metabolites of naphthalene. Young children sometimes ingest moth balls, and in some instances hemolytic anemia and jaundice ensue. A day-old infant suffered such an episode. A medical student asked the mother if she had been eating moth balls, and she said she had during the last trimester of her pregnancy. She had apparently transmitted the metabolites of naphthalene to her baby through the placenta. The mother's blood revealed mild hemolytic anemia. This susceptibility is genetically determined and it was possible by appropriate techniques to detect it in relatives who had never been anemic and who had certainly never dined on moth balls.

People who manifest hemolysis and jaundice after eating fava beans appear to have the same red-cell defect, and one sometimes obtains a history of relatives who have had a similar disease. Here the cultural habits of the family determine the familial nature of the disease, in contrast to that caused by drugs.

The point of this essay may be simply stated. Gene effects, like gold, are where you find them. They may be obvious or they may be obscure. There are many ways to describe them, many levels at which to study them. They are infinitely modifiable, and indeed in each individual, in greater or lesser degree, must be unique; but they are all traceable to that relationship of specificity between the genetic material and those molecules which exert qualitative and quantitative control over the metabolism of the living cell. We are really only beginning to understand the influences of the genes on human variability. The genetic method can isolate and circumscribe the problems to be studied with a high degree of refinement, but it remains for the biochemist to elucidate them.◀

Bull. New York Acad. Med., 35:77-86,1959.

Conjunctivitis: Management with a New Ophthalmic Decongestant

Effective decongestant action was obtained in 96 per cent of 348 patients with allergic conjunctivitis and 89 per cent of 808 patients with various forms of chronic conjunctivitis with tetrahydrozoline hydrochloride (Visine) ophthalmic drops, instilled as 0.05 per cent solution at a dosage of one drop two to four times daily. Relief was prompt and lasted for from one to four hours. The administration of antihistamines, antimicrobial agents or corticosteroids in some patients appeared to enhance the favorable effects of the drug. Except for mild, transient stinging in 2.1 per cent of the patients, no side effects were noted. Although more than 100 patients in the series had cataracts and were treated with the drops for periods of up to two years, none showed any increase in intraocular pressure or significant change in the development of the cataracts.

Menger, H. C., *J.A.M.A.*, 170:178,1959.

The Changing Scene in the Mental Hospital

Better psychiatric services and public attitude have reduced the chronic patient's dependence on hospitals

BERTRAM MANDELBROTE, M.D., *Gloucester, England*

RECOVERY RATE FROM MENTAL DISEASE BETTER 120 YEARS AGO THAN 20 YEARS AGO

During the period 1830 to 1850 there was a remarkably high recovery rate among patients in mental hospitals. Follow-up results at one hospital indicate that 70 per cent of first admissions who had been ill for less than one year were discharged recovered, and that only 20 per cent of these relapsed. At this time the mental hospital was a small unit and the staff consisted of personnel who gave a great deal of their own personalities toward producing an atmosphere which was not so restrictive.

Toward the latter part of the 19th century community attitudes toward mental illness and the zest and zeal for reform in this field subsided. Mental hospitals increased rapidly in size and large numbers of people were admitted which led to overcrowding. Community attitude became more one of exclusion and lack of tolerance of eccentricities in behavior; emphasis was placed on legislation facilitating certification of the mentally ill, prevention of the escape of patients, and other measures for the protection of the public.

At that time in Britain the only way of admission to a psychiatric hospital was by certification. People sought psychiatric advice only when mental illness was fairly advanced or when behavior was such that they

had to be removed from their family setting.

GREATER MEASURES REDUCE VIOLENT BEHAVIOR TO A MINIMUM

If the proper atmosphere is provided in the mental hospital and if community attitudes toward mental illness are healthy attitudes, then disturbed, aggressive and violent behavior is the exception. In a good mental hospital the number of aggressive patients is usually less than 1 per cent and there is little need for restraint.

IMPROVED PHYSICAL THERAPY

Recent advances in physical treatment and the development of tranquilizers have assisted in the management of the acutely disturbed to such an extent that, within a short period after admission, acutely disturbed behavior is rarely seen. Much of the aggressive behavior of chronic patients and the increasing withdrawal and regression, are now thought to be contributed to by restrictive measures, isolation and unawareness of the patients' needs.

ACCEPTING VOLUNTARY APPLICANTS A GREAT ADVANCE

In England and Wales legislation in 1930 permitting the admission of voluntary patients to mental hospitals enabled people for the first time to express a wish to have treatment. It is necessary to provide accommodation which is esthetically pleasing for recent admissions. In several hospitals, the total of voluntary admissions numbers more than 90 per cent. In Gloucester, no admissions within a 20 mile radius of the hospital have been on a certified basis over the past year, and difficult behavior problems are dealt with as a short-term order of three to 28 days.

OTHER CHANGES IN MANAGEMENT OF MENTAL PATIENTS

Adequate classification of patients along behavior lines and organization of patients into small groups for which the total day has been planned is an essential in the development and integration of the hospital community. *Pari passu* with these changes is the need for social and cultural activities and the change of roles within the hospital. By providing a platform for group discussion throughout the hospital structure including patients, medical and nursing staff, as well as technical, administrative staff and other people participating in the functioning of the hospital, it has been possible to deal with the insecurities produced by the change in role and to integrate and cement better interpersonal relationships between these various groupings who tend to guard their own prestige and privileges jealously. By these methods, general apathy and resentments have been changed into energetic, active participation and a healthy approach to problems. Patients have taken more responsibility in hospital management and contributed more to social, cultural, occupational and recreational activities.

Sedation has been markedly reduced; physical assaults have ceased to occur and aggressive behavior between patients have been reduced greatly. Seclusion has dropped from 236 incidents within six months to 10 in a corresponding period. Escapes are about one per week, little in excess of the number prior to the opening of the doors. No instance of violent or aggressive behavior towards the public has occurred; only three of minor disturbances in relation to the community, all of which were tact-

fully handled. This is probably no more than would occur in a random sample of the community as a whole.

TREATMENT OUTSIDE MENTAL HOSPITALS

A large proportion of the psychiatrist's time is now spent in working in general hospital out-patient clinics, seeing patients in their homes with general practitioners, and discussing emotional aspects of their problems with colleagues in other specialties and in general practice. Closer contact between the psychiatrist and the general practitioner is necessary. Close integration is necessary between psychiatric services provided in mental hospitals and welfare services. Much benefit can be reaped by bringing ancillary workers and the general public into the mental hospital, enabling them to understand how it functions and to appreciate the degree of normality of many of our patients, thus assisting in the provision of a therapeutic social and cultural atmosphere within the hospital.

In many British mental hospitals a League of Friends plays a highly useful part in providing additional patient comforts and benefits, promoting good public relations, assisting in occupational and recreational activities and in facilitating of rehabilitation. Chronic patients have been taken on daily outings and entertained by Women's Institutes members for tea. Members of the League of Friends have come into the hospital to organize camera clubs, gardening clubs and other club activities. Personnel skilled in the teaching of domestic science have helped mentally ill housewives to recover or retain their ability to cope with household duties.

The extent of isolation produced in the mental hospital has been diminished. The degree of dependence of the chronic patient on the hospital is also reduced and he is better fitted for return to the normal community.

LENGTH OF STAY IN HOSPITAL

Discharge from a mental hospital may relate more directly to the proximity of the residence of the patient to the mental hospital than to any other factor. The greatest number of chronic patients in one hospital came from areas far removed, where the patient's family had either disintegrated or lost interest and shelved their responsibilities on to the State.

Development of a proper atmosphere within the mental hospital community is of therapeutic benefit to the patient, facilitates easy return of the patient to the community, and produces more understanding attitudes on the part of the public so that illness porduced by psychologic causes can be more readily recognized, tolerated and treated early. In this way the mental hospital is becoming a base for treating the mentally ill not only by physical and psychotherapeutic measures, but by assisting in re-orientation of their attitudes and motives, and preparing them for improved inter-personal relationships.

HALF-WAY HOUSES

In the process of the management of mental illness there are many half-way houses which can assist either in early management or in gradual rehabilitation. These are out-patient clinics, day hospitals, night hospitals, the annexes and mental health centers and social clubs which should be closely linked with the mental hospital and enable ready referral and interchange of facilities.◀

J.M. Soc. New Jersey, 55:422-426,1958.

Exercise in the Treatment of Postural Low-Back Pain

Low-back pain is caused by wrong use of the back or poor body mechanics in most cases

A. M. COHEN, M.D., *Wood, Wisconsin*

In 80 to 90% of cases of backache the cause is postural involving wrong use of the back or faulty body mechanics. Re-establishment of normal balance can be accomplished by exercises, improving body balance and coordinating movements of all the segments.

The muscle imbalances of lordotic posture may be tight low-back muscles, weak abdominal muscles, tight hip flexor muscles, weak glutei and hamstrings—one to all. The housewife who does heavy work in many positions does not protect her back by proper development and use of muscles. Her posture is usually poor with sway back and prominent buttocks, later loss of elasticity in the ligaments. High heels make matters worse. Many sit for hours each day in chairs conducive to poor posture, e.g., a swivel or tilting chair. Obesity's added abdominal weight shifts the center of gravity forward, and to compensate, the upper trunk is thrust further back, adding further tension to the posterior skeletal structures.

The following proposed exercises are best performed on a padded floor:

1. Lying on back with knees bent, the head, shoulders and trunk are raised off the floor, then the trunk is flexed till the floor between the feet

can be touched by the finger tips. By varying the distance of the heels from the buttocks most people can perform this maneuver without stabilizing the feet.

2. On the back, feet flat on the floor, heels nearer buttocks than in 1, the pelvis tilted posteriorly by an active contraction of the glutei maximi. The hands are placed on the abdomen just above the umbilicus and hold the upper abdomen down so that flexion is only at the lumbosacral spine.

3. In the same position as 2, the knees are brought to the chest, hands clasped about the legs, knees are pulled forcibly to the chest. Grip on the knees is not released during the exercise, and the thighs are spread apart to avoid contact with abdomen or chest.

4. In the sitting position, knees extended, the thorax is flexed upon the pelvis and attempts made to touch the toes with the finger tips.

5. Extending one leg backward, with the hip and knee of the other leg flexed to about a right angle, the thorax is flexed over the pelvis, the upper extremities allowed to hang down. The foot of the flexed extremity remains flat on the floor. The foot of the extended extremity is dorsiflexed so that the weight is borne on the ball of the foot and externally rotated. By further flexing the forward knee, the pelvis is moved up and down stretching the tight structures of the anterior thigh which limit extension of the hip joint.

6. The "flat-foot squat," is executed with the heels 12 inches apart, feet turned out at an angle of 30°. The heels remaining flat on the floor, the spine is put through one total curve, with the head bowed and this position maintained until completion of the exercise. The arms, elbows between knees, are pointed toward the floor at a point eight inches in front of the toes, and as the squat is executed the hands touch the floor. This can easily be done at intervals while at work.

The importance of keeping the extension of the lumbosacral spine at a minimum must be impressed upon the patient. Unless he learns to maintain his improved alignment in ordinary, every-day activities, the exercise program will have been in vain.

When standing and walking, the chest should be the part farthest forward, the pelvis tilted posteriorly, feet pointed straight ahead, most of the weight borne on the heels. If it is necessary to stand for a considerable time, high heels should not be worn.

Sit with the lumbo-sacral spine mildly flexed. The driver's seat should be far enough forward so that the knees are in a position higher than the hips.

Sleeping on the abdomen should be avoided. The preferable sleeping position is on the back with the knees elevated. Elevation of the knees can be attained by a roll under the mattress.◀

Wisconsin M.J., 121-125,1959.

Cardiac Arrest and Resuscitation Twice on the Same Patient

Medical personnel should be able to handle cardiac arrest whether it occurs in the operating room or near vicinity

E. E. MIHALYKA, M.D.,* A. M. ZIPPERT, M.D.,* F. SCHILLER, M.D.,* and C. C. R. JACKSON, M.D.,*
Cleveland, Ohio

More and more attention is being focused on the possibilities of cardiac arrest and resuscitation. There are only a few published cases whereby the patient had cardiac arrest outside of the operating room, and recovered with proper and adequate restitution of the oxygen system and cardiac resuscitation.[1-4]

Today, there are thousands of operations being performed in thousands of hospitals and it behooves everyone to know what to do immediately when a patient attains cardiac arrest or ventricular fibrillation. A survey covering the Crile Veterans' Administration Hospital in Cleveland, Ohio, revealed that there were approximately 13,659 surgical procedures during the period of 1953 through 1956, and of this total number of procedures, there were nine cardiac arrests which, when broken down, revealed a rate of one out of every 1,417 operative proecdures. The survey revealed that in each in-

*Crile Veterans Administration Hospital.

1. Dale, W. A., *Ann. Surg.*, 135:376-393,1952.
2. Beck, C. S., et al., *J.A.M.A.*, 161:434-436,1956.
3. Mozen, H. E., et al., *J.A.M.A.*, 162:111-113,1956.
4. Brown, C. D., et al., *J.A.M.A.*, 163:352-353,1957.

stance, the onset of cardiac arrest was in the operating room. Two of the nine patients who had cardiac arrests and immediate cardiac resuscitations are living today. The others have expired from various periods extending from post-operative cardiac arrest up to four months post-operatively.

The procedure must, of necessity, be carried out immediately upon satisfaction to the surgeon or surgeons in the immediate vicinity of the patient that no pulse, blood pressure, or heart sounds are present There is no time for four or five people to come to the conclusion that the patient should be resuscitated. Courage is most important at this particular point, when the patient is in cardiac standstill, and the surgeon must immediately make the necessary incision and, concomitantly, necessary steps must be made to restore the oxygen system to the body. One without the other is of no use to the patient. Oxygen restitution is foremost, because irreparable cerebral damage is done if there is lack of oxygen for a period of time longer than approximately four minutes. Oxygen routed to the system via one hundred per cent oxygen mask, the oxygen nasal catheter, intratracheal tube, or if necessary, mouth-to-mouth breathing and the removal of accumulated CO_2 accomplishes the necessary ventilation.

PRESENTATION OF A CASE

A white male of 63 was admitted on May 7, 1956 with the chief complaint of hoarseness of more than one year's duration. The patient also noted a large lump arising in the right anterocervical region of his neck during the two weeks prior to admission. The patient had been treated for questionable tuberculosis in 1920 and 1940 at a tuberculosis hospital in New York State. The patient's past medical history reveals that he had a hemorrhoidectomy in 1936, and the inactive tuberculosis for which he had been hospitalized both in 1920 and 1940.

Physical examination at this time, revealed a 63 year old, thin, pallid, not too well nourished white male, with obvious hoarseness. There was a palpable mass in the right anterior cervical region, approximately one inch in diameter, which was non-tender, somewhat firm, non-nodular, and mobile. The abdomen was protuberant, soft, and non-tender, and the patient had a right indirect inguinal hernia which was easily reducible. The heart revealed a regular irregularity of rhythm, but there was no enlargement to percussion of any other irregularity abnormality. Indirect laryngoscopy revealed an easily friable, granular mass, which covered the anterior two-thirds of the left true vocal cord, and which appeared to extend about 1.5 centimeters subglotically. Laboratory studies revealed a white blood cell count of 11,500 with a differential count of 69 neutrophils, 10 monocytes, 17 lymphocytes, 2 eosinophils, and 2 basophils. Hemoglobin was 14.35 grams. VDRL was negative. Bleeding time, one half minute; coagulation time, five minutes. Blood was Rh positive. Urinalysis was normal. Hematocrit was forty-five per cent, blood urea nitrogen was 17.2. X-ray revealed the chest to be somewhat emphysematous in type, a mild elongation of the aorta, blunting of the left costophrenic sinus. There was no evidence of any active pulmonary disease. The skeletal survey revealed a small fusiform aneurysm of the abdominal aorta which was calcified.

There was a moderate hypertrophic degenerative change of the lumbar spine, but there was no evidence of skeletal metastases. The patient had a complete cardiological workup and the electrocardiogram revealed a normal record preoperatively except for a marked sinus arrhythmia.

On May 9 the patient had a direct laryngoscopy and biopsy, the result of which was moderately well differentiated squamous cell carcinoma of the left true vocal cord with metastases.

On May 22 the patient was prepared for a total laryngectomy and a left radical *en bloc* neck dissection Pre-operatively, the patient had atropine sulfate gm. 1/150, demerol 100 mg. Both of these were given forty-five minutes pre-operatively, and he had seconal gr. 1½ on May 21 at night time prior to going to sleep, and again at 6:45 on May 22. The patient had sodium pentothal, gas, oxygen, ether anectine type anesthesia, and was intubated. While the patient was being prepared for the radical neck dissection, suddenly his blood pressure dropped to zero, pulse stopped, and there were no heart sounds. Immediately, a circumlinear thoractomy incision, which was bloodless, was made in the fifth intercostal space extending from the sternum to the midportion of the axillary wall, and the hand was thrust into the chest cavity and the heart, which was in standstill, was grasped and in rhythmic manner, massaging of the heart was started. Simultaneously, 100 per cent oxygen was switched on into the intratracheal tube. Approximately 37 seconds later, the heart resumed its normal rhythmic beat. No drugs were used to help resuscitation in this particular instance. The Finochietto chest

retractor was inserted and the heart beating was observed and the patient's chest was left open for approximately 40 minutes. Electrocardiogram was instituted which revealed a return from a cardiac arrest to a normal sinus arrhythmia. Blood pressure returned to 75/55 mm. of mercury. Prior to closure of the chest, the entire field was completely redraped with sterile drapes. The left hemithorax was lavaged with one per cent neomycin solution. A thoracotomy tube was inserted and attached to the under water suction apparatus. Approximately two hours later, the blood pressure returned to 90/60 mm. of mercury, and the ventricular rate was seventy-six. The incision was closed with #0 chromic catgut, and just prior to final closure, the lungs were re-inflated. The skin was closed with #0000 interrupted black silk. The patient was then removed to the recovery room after approximately two hours in the operating room itself.

The post-operative events revealed that at approximately 2 p.m. of the same day, the patient had subcutaneous emphysema over the left upper chest area, and a second thoracotomy tube was inserted into the anterior left third interspace, via trochar, and the patient seemed to improve. On May 31, all the sutures were removed. The patient's remaining convalescent period was uneventful. After talking with the patient and his family, it was decided that a second attempt at total laryngectomy and left radical neck dissection should be made.

Accordingly, on June 5 the patient was properly draped and prepared and this time, having atropine sulfate gr. 1/75, and morphine sulfate gr. ¼, approximately forty-five minutes pre-

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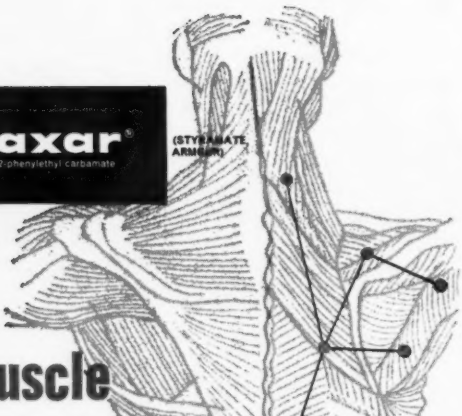

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operatively, and second gr. 1½ on June 4, at night, and again one hour prior to surgery on June 5. This time, the electrocardiograph was attached to the patient prior to any surgical attempt and having everything ready, the patient had just started to be intubated. The blood pressure vascillated around 50 and the pulse vascillated very irregularly between 58-160 when suddenly again he went into cardiac arrest with the blood pressure and the pulse dropping to 0, which was immediately noted. The electrocardiogram showed cardiac arrest and in approximately six to 10 seconds. It was decided that the emergency shock procedure should be instituted with elevation of both lower extremities and the patient was very rapidly intubated and 100 per cent oxygen was instituted. Heavy pressure and chest pounding over the left portion of the chest was employed. The patient came back from cardiac arrest without any surgical or medical intervention in approximately 10 to 15 seconds.

The patient was again observed in the recovery room, and apparently again recovered without any cerebral damage this time as in the previous procedure. The patient was observed for approximately two hours, and monitored with electrocardiogram monitoring machine with the electrocardiogram again returning to sinus arrhythmia. It was felt that after having had two surgical attempts, this patient should be treated by x-ray therapy. The patient had a total of 4472 *r*'s to the right oblique neck region, and a total of 4472 *r*'s to the left oblique neck section. The patient was discharged from the hospital on August 9 without any apparent cerebral involvement. The patient has been

followed at monthly intervals at the Nose, Ear, Throat Follow-Up Clinic and so far, the patient's overall general condition seems to be somewhat improved. The hoarseness is still present. The patient has not gained or lost any weight, but is able to carry out a somewhat seminormal life.

CONCLUSIONS

In the surgical service of Crile Veterans' Administration Hospital during the years of 1953 through 1956, there have been 13,659 surgical procedures. Of this number, there have been nine cardiac arrests and with cardiac resuscitation done in the operating room itself. Of the nine, two are still living, one of the patients having two cardiac arrests with successful resuscitations in both instances.

It is felt that surgeons, anesthetists and medical personnel should be able to handle cardiac arrests, be it in the operating room, or in the immediate vicinity of the operating room. ◀

Reprinted from *Virginia M. Month.*, 86:40-42,1959

Inadequacies of Routine Preoperative Bleeding and Clotting Testing Methods

Many have recommended more attention to the complete personal and family history, and complete physical examination. The patient (or parent) should be questioned regarding relatives who may have bled or bruised easily, or bled excessively from scratches, extraction of teeth, or other operations. The patient should be carefully exmained for bruises and for evidence of disease which might predispose to bleeding..

A deficiency in blood platelets may be detected by examination of blood film, or by a clot-retraction test. If responsibility for the detection of a hemorrhagic state is to rest with the laboratory, the technologist should be given a check list of questions to ask the patient, and should examine the skin and mucous membranes.

If the family and personal history are negative and the patient now has no evidence of bleeding, determination of bleeding and clotting times is not indicated. If the history suggests a tendency to bleed, the patient should have a platelet count, determination of the bleeding time by the Ivy method, and of the coagulation time by the multiple-tube method, as well as observation of the clot. Also desirable are plasma and serum prothrombin activity tests (Diggs).

In a large hospital for children, in 20 years' experience, a physician in charge of the blood clotting research laboratory could not recall one instance in which a *bona fide* hemorrhagic disorder was discovered solely by the use of routine peoperative bleeding and clotting times. In a 3 year period, 28 patients whose bleeding and venous clotting times were normal were proved by more detailed methods to be victims of hemophilia, plasma thromboplastin complement (PTC) deficiency, plasma thromboplastin antecedent (PTA) deficiency, hypoconvertinemia, and fibrinogenopenia.

Careful history and physical examination by the physician are the best methods for determining whether the patient may undergo an operation without detailed study of the clotting mechanism.

Smith, E. B., & Beamer, P. R., *Current Med. Digest* 26:76-77,1959.

Animal Diseases: Their Relationship to Human Health

The economic importance of animals and the many illnesses contracted from animal-carriers make strict control of animal disease imperative

J. D. MARTIN, M.D., *Baton Rouge, Louisiana*

The association of rats with disease of bubonic nature is indicated in the cuneiform writings of Babylonia. A celebrated passage in Susruta is interpreted as indicating that early Indian medicine had knowledge of the relationship between mosquitoes and malarial fever. A warning to abandon a dwelling when its rats act queerly and die suggests to Castiglioni that the ancient Persians and Indians suspected the relationship between plague and rats.

Bubonic plague and louse-borne typhus probably were known to the Romans also. History suggests frequent epidemics of bubonic plague with thousands of persons dying, and Castiglioni tells of the pestilence, called the Plague of Antoninus, or of Galen, that lasted from 164 to 180 A.D. and was probably louse-born typhus, although it could have been bubonic plague.

Kelser quotes Aristotle as writing in the 4th Century B.C., that "dogs suffer from madness which puts them in a state of fury, and all animals which they bite when in this condition become also attacked with madness."

Frightful epidemics of malaria wreaked havoc in Rome in the later period of the Roman Empire, malaria

was associated with swamps and they were drained in an effort to control the malaria.

Epidemics of louse-born typhus have probably occurred everywhere and in every period of history where people have lived under crowded, unsanitary conditions. Blake, et al. believe that it afflicted the natives of south China in the 16th Century. As urbanization developed in the medieval period, the crowding of people into cities and the almost constant military conflict between these cities, with the resultant movement of armies, spread disease everywhere. Zinnser quotes J. F. C. Hecker's estimate that 25 million people died in Europe of this disease during this period.

The development of cities also resulted in the adoption of laws to protect the health of mankind. In 1350 A.D., John II of France established sanitary police as a governmental instrument. Two of the functions of this regulatory force were to keep hogs out of cities and to prevent butchers and fishmongers from selling spoiled meat and fish. After that year, step by step, the sanitary regulations that presently protect man were developed.

About one-half of the people of the world need animal proteins. Unless a concerted effort is made to bring all of the world's technical knowledge, skills, and financial resources into play to control animal diseases and parasites, the present problem will be even greater in the future.

The United States has just waged a successful campaign in Mexico, at a cost of more than 134 million dollars, to eradicate foot-and-mouth disease from cattle. The Mexican government spent a similar large sum of money in this fight, but foot-and-mouth disease is now under control in that country. The vast meat resources of Uruguay and Argentina are barred from the United States because of the danger of importing this disease.

Today, biological warfare is a threat, and a number of the agents that cause animal disease are adaptable to biological warfare. It behooves us, therefore, to become familiar with these diseases in animals and man, to be ready to apply control measures and, in the meantime, to develop faster and more accurate ways of identifying agents of disease and of producing and using immunizing agents.

Ann. New York Acad. Soc., 70:280-291,1958.

Intrathoracic Meningocele

Twenty-seven such cases have been collected from the world literature. These were 14 female and 10 male patients between the ages of 7 weeks and 63 years, and in 3 patients with incomplete data. Two additional cases of intrathoracic meningocele are cited, one in a man of 44, and one in a woman of 37. Fourteen of the 27 patients had surgical correction. Four of the 14 died of causes directly related to the operation. Two patients had myeloplasty and recovered with satisfactory results. Intrathoracic meningocele is to be suspected whenever a posterior mediastinal tumor is discovered along with skeletal changes and neurofibromatosis.

Hilton, H. D., & McCarthy, H. H., *J. Thorac. Surg.*, 37:261-268,1959.

Incidence of Gallstones in 1,233 "Normal" Men

X-ray studies of a large series of presumably normal men revealed an incidence of gall-bladder abnormality of 14.6 per cent of the 1,233 cases observed.. Equally surprising was the unexpectedly high percentage (70%) of patients with gallstones but without symptoms.

The study, done with the cholecystographic medium Telepaque, an oral contrast agent administered the night before the films were made, demonstrated normal biliary function in 85.4 per cent of the patients, 14.6 per cent with evidence of present or past gall-bladder abnormality. Most men in the series were active business men in age from 35 to 55 years, fairly typical of employed U.S. males in the same age range. Women have an even higher percentage of silent gall-stones. It is further noted that the incidence of gallstones rises sharply after retirement.

Wilbur, R. S., & Bolt, R. J., *Gastroenterology*, 36: 251,1959.

Asthma, Eczema, Urticaria, Rhinitis Syndrome

Almost all physicians encounter patients of this type. Discouragement with the results of therapy leads some of these patients to desert the allergist in favor of symptomatic treatment. When this fails, the patient returns to the pediatrician, the generalist, or the internist. All of these conditions present in a patient at any one time is the exception. The natural history of the syndrome is one of progression and alteration. A baby with eczema loses the skin lesions and, later on, seasonal allergic rhinitis and/or asthma develops.

Our psychiatric colleagues are helpful with many of these cases, but public facilities are overloaded and private offices often are too expensive for all but a few patients. Furthermore, dividing the patient between two physicians with different ideas of management often leads to confusion resulting from the practical difficulty of communication between the two. Perhaps the best solution to the problem is the employment of a qualified psychologist or psychiatric social worker to work in the allergist's office. The patient is seen by the psychologist for an hour once a week, and allergy therapy is given at this same visit. Symptoms which may have occurred in previous days are investigated with the object of unveiling tensions which have induced symptoms, and the allergist gives advice.

Each case must be judged by itself. One must abandon an "either/or" attitude, and must not resist the inevitable wedding of allergy and psychiatry. It is better to accede and spare the patient the unhappiness of quack nostrums, and wandering about in

search of magic cures, or a completely dry climate. The allergist should be as well prepared to undertake limited psychotherapy as to perform skin tests. Any other physician who undertakes the care of these patients should be well trained in both these techniques. The patient (or parents) must have as much confidence in the physician who discusses feelings as in the one who discusses ways to avoid cat dander. Successful control of all the manifestations of the asthma, eczema, urticaria, rhinitis syndrome is not a Utopian dream, but a goal within reach of all who avail themselves of our current knowledge in the fields of allergy and psychiatry. Psychoanalysis is for the few who will not respond to lesser measures.

Tuft, H. S., *Pennsylvania M.J.*, 62:177-180,1959.

Abdominal Pain

The Roman, Caelius Aurelianus, was the first physician who believed intestinal pain to be caused by distention of the lumen of the viscus. Vesalius of Padua (1514-1568) was the first anatomist who described connections between the abdominal viscera and the sympathetic trunk, and between the sympathetic trunk and the spinal nerves. Eustachius of Rome (1520-1574) confirmed the findings of Vesalius, and Thomas Willis of Oxford (1621-1675) further elaborated on the structure of the sympathetic nervous system, showing a "solar plexus" in the center of the abdomen as the origin of many radiating nerve branches into the mesentery.

Morgagni of Padua confirmed this sensibility of the intestines when inflamed or in spasm, and demonstrated the insensibility of the visceral peritoneum to pinching or squeezing, and the Dutchman, Reil, in 1807, concluded that the visceral innervation is not dominated by the *cerebrum abdominale* (celiac plexus) as is the cerebrospinal nervous system by the brain.

Hilton (1880), Ross (1888), Head (1893), Lennander (1907), and McKenzie (1920) all showed conclusively the insensibility of the abdominal viscera to pain stimulation unless they were acutely inflamed, there was tension on the mesentery, or the lumen was forcefully distended. They found pulling or pinching of the mesentery painful under all circumstances.

In a typical appendicitis the initial lesion causes a stream of afferent impulses via the autonomic nervous system towards the cortex. The pain is poorly localized and felt in the abdominal mid-line about the umbilicus. However, the pain also sensitizes the whole organ system and influences affect, emotion, and personality in general, so that the easily excitable patient will have a much lower sensory threshold, while the stoical individual might well have sand in the synapses. Thus pallor, nausea, and sweating are generalized effects of a local pain stimulus.

Depending on the anatomic location of the appendix, peritoneal irritation is likely to result sooner or later, either by contact with the viscus or by direct extension of the inflammatory process. Then, instead of periumbilical pain, there develops a steady, accurately placed pain and local guarding of the abdominal musculature with a positive rebound test. The latter symptoms are all the result of somatic sensory irritation in the peritoneum and abdominal wall

Should the appendix rupture, spilling of the infectious contents throughout the peritoneal cavity would then result in a widespread somatic as well as visceral response. It is somatic in the form of a boardlike abdomen, splinting of the respiratory movements, and intense abdominal tenderness. It is visceral in the form of paralytic ileus and vomiting combined again with acute tenderness of the entire intestinal tract.

Kohler, F. P., *Pennsylvania M.J.*, 62:67-69,1959.

Steatorrhea

Steatorrhea, the main clinical syndrome of malabsorption from the small intestine, can be due to four often closely interwoven mechanisms:

1. Inadequate mixing of food and intestinal secretions.
2. Diminished supply of biliary and pancreatic secretions.
3. Disorders affecting its secretory and absorptive efficiency.
4. Abnormal bacterial activity in the small intestine with competition for essential nutrients.

The stomach acts as a reservoir, permitting orderly emptying into the small intestine and stimulation of the pancreatic and biliary secretions. Loss of this hopper mechanism is probably the primary cause of malabsorption in the intestine associated with partial gastrectomy and particularly with total gastrectomy. Bile and pancreatic secretions chase the food down the intestine instead of merging with it.

Steatorrhea has been described as due to a failure of bile salt production only, and it is possible that other cases are primary loss of a single component of the digestive juices. It has been found with gross gastric hypersecretion of acid.

Malabsorption must clearly follow if there is an insufficient absorption area of small intestine. This can be due to surgical extirpation of intestine, short-circuiting of intestine either surgically or by nature, producing an internal fistula which can happen from inflammation of a diverticulum of the intestine, or from perforation of a peptic ulcer. Absorption from the intestine must be reduced if the mucosa of the intestine is damaged by a disease process, or if local disease of the part causes a hold up. So-called idiopathic steatorrhea has now been shown conclusively to be associated with diffuse atrophic changes. The final mechanism is the disturbance of intestinal function due to the presence of abnormal bacterial flora in a stagnant loop or pouch in the intestine—the "blind loop" syndrome.

Steatorrhea in its florid form is easy to recognize but the secondary causes must be exceeded. The diagnosis should be considered when there are intermittent bouts of loose stools, or watery diarrhea lasting for a few days and recurring several times a year. Constipation may exist between such attacks, intermittent nausea and vomiting may be a main feature and, as gastric stasis may occur, pyloric stenosis may be misdiagnosed. The clinical picture of Addison's disease with weakness and skin pigmentation may be closely mimicked.

The diagnosis rests on the demonstration of increased fat excretion by 3-day stool estimations, finding more than 6 gm. a day on a normal dietary intake, confirmed by the demonstration of a histologically abnormal jejunal mucosa, and a good response to a gluten-free diet.

Jones, F. A., *Proc. Roy. Soc. Med.*, 52:38-42,1959.

Allergy of the Nose and Paranasal Sinuses

It is estimated that 80% of patients with chronic sinusitis are allergic, since nasal smears in this percentage exhibit a high percentage of eosinophiles. The simple classification of allergic rhinitis is into the seasonal (hay fever) and the perennial form. Hay fever is due solely to pollens, perennial rhinitis to the allergens which also cause year-round bronchial asthma—house dust, foods, and animal and miscellaneous derivatives including insects, insecticides and occupational dusts. There is increasing awareness of the importance of molds, smuts and other fungi. Molds and smuts are prevalent outdoors in summer, but molds are also found in the home all year round, especially in damp basements, rugs, carpets and furniture, and are therefore capable of causing both seasonal and perennial allergic rhinitis. Molds and smuts may be in the air simultaneously with the pollens of trees, grasses and weeds so that many allergic individuals require simultaneous desensitization therapy for both.

The severity of symptoms of allergic rhinitis varies with sensitiivty of the patient, and degree and duration of exposure. The nasal mucosa is a continuation of the one lining the eight parnasal sinuses, any part of which cannot become infected without involving the other parts to some degree. Usual symptoms include sneezing, rhinorrhea, nasal obstruction, itching of the roof of the mouth and nose, and conjunctivitis. Since hay fever fungus allergy seasons vary little from year to year for any location, most hay fever patients give a history of rather strict adherence to the same dates, year after year, provided there is no change of residence. Symptoms in these cases increase with high pollen counts. Nasal polyps occur very rarely in those patients who have only one type of hay fever, whereas the "perennial" patient has nasal blocking, sneezes, has watery nasal discharge, and some dulling of the sense of smell. Conjunctivitis in perennial patients is rare, itching mild or absent. The nasal mucosa is pale, often glistening and watery, and the nose obstructed to a greater or lesser degree. The persistent edema sags the mucosa to form "polypoid" tissue, and if continued, actual polyps. These are not tumors in the ordinary sense, but waterlogged, hanging down bits of mucous membrane. The patient's family may be allergic, he may have other allergies, his skin tests usually are positive, and his nose looks allergic.

Rhinitis due to fungi constitutes a year-round problem. In hay fever the diagnosis is rarely difficult. Complete skin tests should be made to confirm the diagnosis and to discover all possible causes. Scratch tests are recommended initially. If all answers are not discovered, 20 to 60 intradermal tests with allergenic extracts negative with the scratch technic are employed. The history pays special attention to home contents. Skin tests should not be made if an antihistaminic has been taken in the preceding 72 hours. Epinephrine or ephedrine may cause false negative skin tests.

For nasal examination the room must be dark, the examining light must be bright. The speculum should be as wide as possible. Dilation by spray, e.g., ¼% Neo-Synephrine may be necessary, but only after the material for nasal smear is collected.

Unger, L., *West Virginia M.J.*, 55:122-125,1959.

briefs: SURGICAL

Hypophysectomy in the Treatment of Metastatic Breast Cancer

A total of 218 patients were subjected to this operation over a period of 4 years. The results in the first group of 109 patients who had a minimum follow-up of 17 months are presented, and data on the second group of 109 are considered to some extent. Most patients were ambulatory in 24 to 48 hours. The average hospitalization was 10 days. Hormonal replacement therapy was 37.5 mg. of cortisone and 120 mg. of desiccated thyroid, by mouth, daily. Posterior pituitary powder, by nasal insufflation, was required in some cases for control of thirst and polyuria. During periods of stress an increase of cortisone was required. Patients who have had hypophysectomy have a normal appearance and the mental and physical functions are normal. The mortality rate from all causes was 7.3%. Only one death in the second group of 109 patients was directly attributable to the operation. Autopsies revealed extensive metastases in the 8 patients in the second group who died postoperatively. Of the first group of 109, 50% had objective remissions, and 35% had remissions of 6 months or longer. A prior favorable response to oophorectomy was found to be of prognostic value.

Pearson, O. H., & Ray, B. S., *Cancer*, 12:85-92,1959.

Use of a Steroid Ointment for Debridement

A man of 45 had a necrotizing infection which had destroyed the dorsal foreskin and produced a 2.5x1 cm. ulceration just proximal to the glans penis. The surface of the ulcer was moist, foul, and consisted of dense, adherent, necrotic tissue. A steroid ointment containing an antibiotic was applied three times a day to reduce the swelling. In two days the necrotic tissue was loose and six days later all necrotic tissue was gone and a clean defect extended through the skin to the fascia covering the corpora cavernosa.

Steroid ointment achieved separation of necrotic tissue in areas of moist gangrene in several cases. The mechanism is not known; apparently the cohesion between dead and living tissue is destroyed and the dead tissue falls off. When any steroid ointment is applied to large raw areas, there will be some absorption into the systemic circulation. Signs of hypercortisonism—increase in appetite and weight and change in psyche—should be watched for in these patients.

Any cortisone will stop the proliferation of fibroblasts without interfering with the growth of epithelium. If the necrotic ulcer is superficial, epithelium will cover the defect during treatment with the steroid ointment. If the defect extends deeply into or through the dermis the steroid

will interfere with formation of granulation tissue and stop healing. Under these conditions the steroid ointment should be used only as long as necrotic tissue is present and then be replaced with stimulating therapy.

Although every treated area in this patient was superficially infected there was no spread into living tissue. An ointment containing neomycin was used as a safeguard against this dissemination. The steroid had no effect upon the barrier which was preventing the spread of bacteria. Only a single steroid ointment was used because it was difficult to obtain enough patients for adequate study.

Becker, S. W., & Brennan, B., *J. Indiana M.A.*, 52:513-515,1959.

Spontaneous Internal Biliary Fistula

The added complications of ascending infection, hemorrhage or gallstone ileus among these patients urge surgical correction, but the mortality rate is discouragingly high. Earlier treatment of gallbladder disease and constant suspicion of fistulae will aid these unfortunate patients. Spontaneous internal biliary fistula occurred seven times among the first 160 patients who had operations upon the biliary tract.

These fistulae are usually recognized in the sixth and seventh decade. Formation begins with cholecystitis, followed or preceded by cholelithiasis, and subsequently pericholitis with adhesion formation. Gallstones are the cause in 90% of all cases, perforating peptic ulcer in 6%, carcinoma in 4%.

The most frequent complication is bacterial infection. Regurgitation of gastrointestinal contents into the biliary tract may occur with subsequent development of cholangiohepatitis and, in time, there may be widespread intrahepatic scarring or abscess formation. Gallstone ileus is a frequent complication. Internal hemorrhage from erosion by a gallstone may cause severe blood loss.

These fistulae are not common, but their mortality rate is high. Of the seven patients operated on, two died. There is need for a better understanding of the etiology, diagnosis, complications and treatment of gallbladder disease. Infection, hepatic insufficiency, and other secondary complications should determine the choice of surgical management. Of greatest importance is the realization that staged remedial procedures may save the patient to later withstand radical cure of the fistula.

Wall, N. R., & Smith, G. A., *Missouri Med.*, 56:523-529,1959.

Crohn's Disease

Of a total of 48 males and 60 females, aged 4 to 69 years at time of operation for regional ileitis (Crohn's disease), 52 have been followed for more than 5 years and 30 for more than 10 years. The recurrence rate for patients who had symptoms for more than 2 years before operation and followed for more than 5 years was 65%. Of those with symptoms for less than a month before operation, only 12% have suffered a recurrence. Of the patients with symptoms from one month to 2 years, and followed for more than 5 years, the recurrence rate was more than 22%. Once the disease has recurred, it is unlikely that it can be brought permanently under control by any means, medical or surgical.

Pollock, A. V., *Brit. J. Surg.*, 46:193-206,1958.

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References: 1. Finkelstein, M., et al.: J. Pharmacol. & Exper. Therap. 125:330 (April) 1959. 2. McHardy, G., et al.: Postgrad. Med., in press. 3. Winkelstein, A.: Amer. J. Gastroenterol., in press. 4. Finkelstein, M., et al.: Presented at Fall Meeting, Amer. Soc. Pharmacol. & Exper. Therap., 1958. 5. Leming, B.: Clin. Med. 6:423 (March) 1959.

*Trademark

New Technics for Diverting Spinal Fluid Flow in Congenital Hydrocephalus

The causes of failure of procedures for cure of hydrocephalus have been:

1. Resultant meningitis.

2. Obstruction to the flow at the distal end of a prosthetic tube.

3. Electrolyte imbalance due to continued loss of cerebrospinal fluid.

4. Hydrostatic imbalance of cerebrospinal fluid within the central nervous system.

5. Interference with physiologic process in other organs of the body.

During the past 18 months two methods for diverting the cerebrospinal fluid have been used in the treatment of 14 patients.

The ventriculobiliary shunt was introduced after the development of a suitable flutter valve which prevented the reflux of bile and was also resistant to various chemicals. The gallbladder was selected because it best met the criteria for allowing the persistence of a shunt, relative sterility, ample resorption of electrolytes and water, hydrostatic pressure to maintain intracranial pressure at a suitable level, the gallbladder not being an essential organ, and bile a lytic substance preventing a fibrous reaction to plug the distal end of the tube.

In the communicating hydrocephalus the shunt is made between the high lumbar subarachnoid space around the right flank into the peritoneal cavity with the valve held in place in the gallbladder by purse-string sutures. In the obstructive hydrocephalus direct shunts from the ventricles may be established, otherwise a Torkildson shunt followed by a spinal subarachnoidbiliary shunt can be made.

In 1957 the Heyer valve which could be placed in the right auricle *via* the internal jugular vein was described. Silicone rubber is used for the shunt. The tube has two parts—the cardiac end has a silicone slit-and-core valve molded into its tip which is threaded into the right auricle *via* the internal jugular vein; the ventricular end is placed into a lateral ventricle through a posterior parietal burr hole, brought subcutaneously behind the ear into the neck where the two portions of the shunt are sized and joined with a small connector made of tetrafluroethylene. The presence of the catheter within the auricle may be demonstrated by x-ray, utilizing the injection of a small amount of a contrast medium.

This procedure causes a minimum of trauma, is not apt to lead to meningitis and the swirl of blood in the auricle reduces the hazard of clotting about its tip. It is easy to remove the cardiac end of the catheter, clean the valve and reinsert it into the old tract. Four revisions have been required in the series to date. Despite the valve, reflux of blood may still cause failure of function.

Experiences with this method are encouraging. Insertion of the catheter and repair of a myelomeningocele have been done in one operation in two instances. One patient, a 14 year old boy, had obstructive hydrocephalus due to a medulloblastoma. Postoperative development of a cerebrospinal fluid fistula and failure of a Torkildson shunt to function required the employment of the Heyer valve. It will remain to be seen if widespread metastasis of this tumor occurs..

Owens, G., *J. Tennessee M.A.*, 52:125-128,1959.

briefs: THERAPEUTIC

Trifluoperazine in Paranoid Schizophrenia

A trial of trifluoperazine was made on a series of 50 patients suffering from acute and chronic paranoid schizophrenia.

In Group A were 30 men with chronic paranoid schizophrenia hospitalized for at least two years. All had been previously treated by methods such as I.C.T. and E.C.T., and a prolonged trial with chlorpromazine and, in many cases, other available tranquilizers. None of these treatments had materially altered the clinical picture. The duration of the illness was two to 14 years.

In Group B were 20 patients admitted during the first attack of schizophrenia of less than six months' duration who had not had previous treatment, with a recommendation for I.C.T. by other consultants.

Suspending all other drugs, 5 mg. of trifluoperazine was given daily for three days, thereafter increasing by 5 mg. daily at three day intervals until gross side effects or a satisfactory result were obtained. The symptoms controlled, the dosage was reduced to a level of freedom from side effects and when therapeutic effect seemed maximal. The maximum dose used was 45 mg., average maintenance 20 to 25 mg., daily. Those discharged have been mantained on 5 to 20 mg. daily..

No patients in Group B have reported a relapse. Three in Group A had a return of symptoms when they had difficulty in obtaining the drug, but they responded when the drug was recommenced. All have been out of the hospital for from five to nine months.

The most troublesome side effects, drowsiness and restlessness, were treated by amphetamine, barbiturates and antihistamines without benefit. Benzhexol hydrochloride, in doses of 6 to 8 mg. daily, proved effective against Parkinsonism and greatly decreased restlessness.

In Group A the greatest effect was on aggression and general overactivity, next auditory hallucinations, then delusions. There was often a remarkable return of insight. Improvement was first gradual, later rapid. An adequate program of rehabilitation remains fundamental to the treatment of schizophrenia.

The only side effect that gave rise to anxiety was motor restlessness. Certainly large doses of drugs should not be given initially except under good day-to-day observation..

MacDonald, R., & Watts, T. P. S., *Brit. M.J.*, 1:549-550,1959.
1:549-550,1959.

Trypsin in Peripheral Vascular Diseases

Researchers reported in 1952 that clots were lysed when trypsin was given intravenously and that the signs and symptoms of inflammation

attending a clot disappeared before the clot itself. A single case of thrombosis of the aorta was treated with very large doses of trypsin intravenously, with a return of brachial pulse by the fourth day. Trypsin was given intra-arterially to patients with severe thrombophlebitis and all symptoms disappeared in 24 hours. Thrombi were not influenced by trypsin administered intravenously, although inflammation cleared rapidly in trypsin-treated patients as compared to a parallel series of patients on anticoagulants. Other clinical studies have confirmed these findings.

Two hundred ten patients with peripheral vascular diseases, mostly of the lower limbs, were all ambulatory and all treated in the office. Crystalline trypsin and a 5% aqueous gelatin menstruum was made up and used immediately. Any residual was stored under refrigeration and used at the next office visit. Injections of 0.5 ml. containing 2.5 mg. of trypsin were given into the deltoid muscle in all but a few patients who required many injections. In these cases the gluteal muscle was used. The arms were alternated, and an area showing signs of a previous injection avoided. During the acute phase of each of the diseases trypsin was given once daily. Later the dose was reduced to 2.5 mg. three times a week until discharged. Other measures used as indicated were antibiotics, hot compresses, elastic bandages, and whirlpool baths.

Of the 42 patients with uncomplicated varicose ulcers, results were excellent in 41, good in 1. Of the 33 with superficial (segmental) venous thrombosis, all responded well and results were graded excellent—complete dissolution of the thrombus and recanalization of the veins or vein. Subsequent surgical ligations and excisions were performed three to six months following recanalization.

Of the 210 patients, 60% had thrombophlebitis, given in three subgroups:

1. Chronic thrombophlebitis with lymphedema, 47 patients. Response excellent in 17, good in 29, and poor in 1.

2. Thrombophlebitis with ulcers, dermatitis, and/or cellulitis, 67 patients. Eleven had two of the complications. Response was excellent in 52, good in 10, and poor in five.

3. Subacute thrombophlebitis with venospasm, 15 patients. Redness, heat, and local thrombosis, cordlike veins of the superficial saphenous system were present. In 12, response was excellent and in three good.

Six patients with leg ulcers not on a venous basis were treated. In five, response was excellent, in one good. Sufficiently large numbers are included in each group to afford information for comparative analyses as to age and sex distribution, number of treatments required and results. Encouraging results were obtained in patients with chronic varicose ulcers, superficial venous thrombosis, acute phlebitis with ulcers, dermatitis and/or cellulitis, and acute superficial thrombophlebitis. Fair results were obtained in cases of chronic deep thrombophlebitis with lymphedema. Irreversible tissue changes may make access of the thrombolytic and antiphlogistic actions of trypsin difficult. Two patients manifested generalized urticarial reactions, and there were local reactions in 14% of the patients necessitating discontinuation of trypsin injections.

Murphy, H., *New York J. Med.*, 59:1973–1980,1959

Acenocoumarin in Coronary Artery Disease

Since Dicumarol (bishydoxycoumarin) was first used clinically 16 years ago, the use of anticoagulants has become a generally accepted procedure in the treatment of certain cardiovascular diseases. The use of these drugs is complicated by several factors, mainly bleeding, which necessitate a very close control over any program in which these drugs are used. Several different drugs have been developed in the search for an ideal anticoagulant.

At present, two types of anticoagulant drugs are being used. The injectable group, typified by heparin sodium, rapidly lengthens the clotting time by interfering with the action of thromboplastin and thrombin, and is excreted in the urine. The oral group is typified by coumarin and indanedione substances which prolong the prothrombin time.

Acenocoumarin (Sintrom) was used in the treatment of 10 patients, all complaining of chest pain, exhibiting electrocardiographic changes compatible with myocardial infarction with two exceptions, all showing significantly elevated sedimentation rate and with three exceptions, all showing significantly elevated serum transaminase. Prothrombin time determinations were done each morning by the plasma dilution method.

Sintrom, in the initial dose of 20 mg., was given concomitantly with 200 mg. of Depo-Heparin. Thereafter, dosage was determined by prothrombin time values. Therapeutic ranges were achieved by the third day in all cases. While the average maintenance dose from person to person showed a wide variation, the individual dose, with two exceptions, was reasonably constant after four to seven days on the drug in one daily dose.

Difficulty in anticipating therapeutic levels was minimal. The drug was found to be effective in small doses. No hemorrhagic or other toxic phenomena were encountered.

Strom, C. H., et al., *J. South Carolina M.A.*, 55:123-127,1959.

Vancomycin for Severe Staphylococcal Infections

Vancomycin was used in the treatment of nine patients who suffered from severe staphylococcal infection of the blood stream, lungs, or operative wounds. Hospital patients are not uncommonly infected by strains of staphylococci that are resistant to four or five of the antibiotics to which this species is normally sensitive. Vancomycin, from Streptomyces orientalis is bactericidal for Gram-positive cocci. The numerous strains of Staph. pyogenes tested against it have been almost invariably sensitive. Neither cross-resistance with other antibiotics nor the development of material degrees of resistance *in vitro* has been found. The drug is poorly absorbed from the intestine. The current preparation is too irritant for intramuscular injection, and, in any case, the drug is not well absorbed by this route and must be given intravenously. The method of intravenous administration least likely to cause thrombophlebitis is by infusion in 250 ml. of diluent over 30 minutes or, where applicable, by admixture with a salient or 5% dextrose drip. Because of the need to give the drug intravenously, and because of its toxicity, vancomycin is at present mainly used for severe staphylococcal infections in the hospital.

Eight of nine patients who were

treated with vancomycin had failed to respond to other antibiotics. Severe loss of auditory acuity followed treatment in several patients.

Vancomycin was given intravenously in 20 ml. of saline over a 5 minute period; by infusion in 250 ml. over a 30 minute period or with larger volumes of saline or glucose through a vena cava catheter over several hours. The total dose was 1 to 2 gm., except for Case 3, and was given as two equal 12 hourly doses. No patient received vancomycin for longer than 15 days, and the maximum course was 22 gm.

The infecting strains of Staph. pyogenes were all resistant to several antibiotics, and treatment with other antibiotics had failed. Two patients died when vancomycin was withdrawn before the infection was controlled. Two others recovered from the staphylococcal infection but died subsequently of Ps. pyocyanea septicemia. Three of the survivors continued to harbor the infecting staphylococcus in lesions.

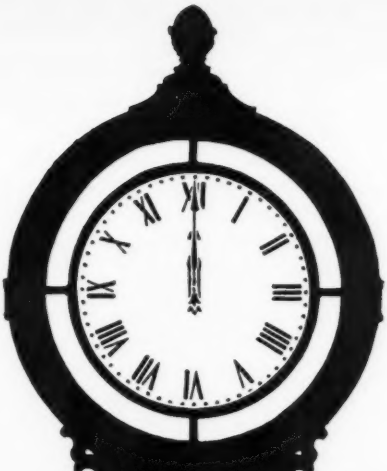
Several uremic patients developed toxic deafness on a dosage of 1 to 2 gm. daily, although none received more than 13 gm. in the course. A regimen of lower doses controlled by rapid serum assays was used successfully in the management of a uremic patient with staphylococcal pneumonia. The drug must be given intravenously, and as it is also toxic to the eighth nerve it is likely to be used mainly in the hospital for severe staphylococcal infections. This is especially true where this organism is resistant to several other antibiotics or where other chemotherapy is otherwise unavailing. It is also valuable when a bactericidal drug is particularly desirable, that is in staphylococcal infections in patients whose normal defence mechanisms are defective.

Dutton, A. A. C., & Elmes, P. C., *Brit. M.J.*, 1:1144-1149,1959.

Disseminated Lupus Erythematosus

Of 125 patients with this disease for at least 8 years, 100 were treated with corticosteroids. The remaining 25 "controls," treated before the advent of corticosteroids, had vitamins, analgesics, and colloidal gold sulphide. All 25 died within 2 months to 2 years from appearace of symptoms.. In those treated with corticosteroids, the time between appearance of symptoms and entry to hospital varied from a few weeks to a few months. Cortisone was given in an initial dose of 200 to 500 mg., followed by doses of 6.25 to 12.5 mg. sustained for a period of 1 to 8 years. Prolonged treatment improved general symptoms, joint pains, and skin lesions in 67, 81, and 72% of the cases, respectively. All other symptoms of lupus remained unchanged or worsened. Thirty-three patients discontinued treatment during an apparent cure or remission; 9 did not report; 19 had recurrences 1 month to 6½ years after discontinuation of treatment; 5 were still under observation, condition excellent, 5 to 7 years after discontinuation of treatment. After 8 years, of the whole group of treated patients, 8 had discontinued treatment, 50 with severe and moderately severe disease had died, and 42 are living and continuing the treatment. It is concluded that corticosteroid treatment lowers the death rate from 100% not so treated to 54% in those treated.

Jalil M., et al., *Rev. med. Chile*, 86:717-732,1958.



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Therapeutic Uses of Gamma Globulins

Gamma globulin is never given intravenously. Intramuscular injections provide a peak serum level by the second day. When large doses must be given, injections may be divided into doses of 10 to 20 ml. per injection site, and given at successive daily or weekly intervals. Toxic reactions are uncommon.

There are, in general, four clinical situations in which it may be beneficial:

1. The syndromes manifested by agammaglobulinemia.

2. The prevention or attentuation of several infectious diseases to which the non-immune person has recently been exposed, *e.g.*, measles, German measles, infectious hepatitis, poliomyelitis, smallpox and pertussis.

3. The prevention of a severe complication (such as mumps orchitis) of clinically established disease control of infection when sufficient specific antibodies fail to develop against the infecting organism, as in progressive caccinia.

4. Control of infection when normal defense mechanisms are depressed, or a disease in which the administration of specific antitoxin is necessary, but unavailable, or in which an antitoxin of animal origin is contraindicated.

Gamma globulin has been proved effective in the prevention of severe recurrent bacterial infections in transient agammaglobulinemia of infancy as well as the congenital and acquired forms of the disease. Antibiotics have been more effective than gamma globulin in terminating any specific infection, but not in long-term prophylaxis. In some cases both antibiotics and gamma globulin have been required.

For the prevention of bacterial infection in persons with agammaglobulinemia, at least 150 mg. of gamma globulin must be injected, 0.45 ml. per pound of body weight, and repeated a few days later. After this the calculated dose of 0.3 to 0.45 ml. per pound of body weight can be given at monthly intervals. It is well to see each patient monthly for the first few months, and to take a serum sample before each therapeutic injection for determination of a gamma-globulin level to see what dose is necessary to keep the serum level above 150 mg. per 100 ml.

Eczema vaccinatum has a 30 to 40% mortality during the first two years of life. Hyperimmune gamma globulin has given encouraging results, prophylactically and therapeutically.

In addition to its usefulness in the general prevention of bacterial infection in patients with agammaglobulinemia, gamma globulin has proved helpful in the prophylaxis and therapy of a variety of specific bacterial infections. The injection of 2.5 ml. of hyperimmune antipertussis gamma globulin, with a dose repeated five to seven days later, has prevented pertussis in 75% of nonimmune children who were exposed. It should be given as early in the incubation period as possible, may be used in larger doses in the treatment. From infections due to Staph. aureua, S. typhimurium, Pseudomonas aeruginosa and proteus, evidence suggests that protection is afforded by its specific antibody content.

Gross, P. A. M., et al., *New England J. Med.*, 260: 170-177, 1959.

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CHARLES J. FRANKEL, M.D., LL.B., *Editor*

▶Is a doctor a qualified expert witness in a malpractice action against a chiropractor?◀

This question was passed on by the Supreme Court of Oregon in 1959 (*Sheppard* vs *Firth*, 334 P. (2d) 190). Plaintiff, whose lower back had pained her for ten years, consulted defendant chiropractor who diagnosed her difficulty as a displacement of the atlas vertebrae and prescribed manipulation. After nine treatments, plaintiff's back became more painful and she consulted an orthopedic surgeon. His diagnosis was subacute muscle strain in the lumbrosacral area. At the trial, the orthopedist, untrained in treating ailments through chiropratic adjustments, testified the chiropractor's treatment was improper and had aggravated plaintiff's condition.

Defendant contended the orthopedist was not qualified to testify as an expert witness against him. The Court said that, in a malpractice action, a physician or surgeon is entitled to have his treatment of the patient tested by the rules and principles of the school of medicine to which he belongs and not by those of some other school. An exception to this general rule arises whenever the methods of treating a particular ailment are generally the same in either school or where the doctor, although trained in one school, steps out of the practice of his own school and attempts to treat

the patient in a manner practiced by another school. Neither exception applies here. The reason for the general rule is that a person who seeks treatment from a practitioner of a particular school agrees to accept the curative practices and beliefs of that school and if the practitioner treats the patient, in accordance with such practices and beliefs, in a reasonably skillful maner, he is not liable. The general rule applies to drugless practitioners; the courts are not concerned with the merits of the various systems of medicine. Many believe in the efficacy of drugless treatment and use the services of those giving such treatment. It would, said the Court, be unfair to permit the treatment of a practitioner of one school to be judged by the principles of another school.

►May a hospital, receiving considerable governmental financial assistance and some immunity from taxation, limit a duly licensed doctor's right to practice therein as he had in the past, without regard to his qualifications?◄

The Superior Court of New Haven County, Connecticut, decided this question in 1958 in *Edson* vs *Griffin Hospital,* 144 A.(2d) 341. Plaintiff, a duly licensed doctor, became a staff member at defendant hospital in 1943. Until 1954 he treated patients there and, assisted by other surgeons, performed certain operations there. In 1954, as the result of the adoption of new hospital by-laws, rules and regulations, he was denied the use of hospital facilities for the performance of certain operations.

Plaintiff contended the hospital is a public institution and that he and his patients are, therefore, entitled to the hospital's facilities as a matter of right. Thus, said the Court, the basic question is whether defendant is a private corporation operating a nonprofit hospital or a public corporation operating a public hospital. Under the act incorporating it, the hospital, a nonprofit organization, is empowered to make rules and regulations necessary for its management and to select a board of trustees which can conduct all its business and appoint and remove, as necessary, servants, officers and agents. The hospital receives state aid, special grants from surrounding towns and contributions from charitable funds. However, 95% of its income is derived from services rendered.

The Court said it has long been recognized that a public corporation is an instrumentality of the state, founded and owned in the public interest, supported by public funds and governed by those deriving their authority from the state. A corporation organized by permission of the legislature, supported largely by voluntary contributions, and managed by persons who are not representatives of any political subdivision, is a private corporation, even though it engaged in charitable work or performs duties similar to those of public corporations. A private hospital is one in which no governmental body has a voice in managing its property or formulating rules governing its operations. The mere fact that a hospital receives money from political subdivisions or charitable funds does not change it from a private to a public hospital.

Plaintiff doctor argued that in many instances courts of the state have referred to hospital as "public hospitals" or "public institutions." Agreeing this was true, the Court pointed out that in each instance the particu-

lar problem in issue had to be taken into consideration. When tax or general liability questions are in issue, hospitals are properly characterized as public institutions. But such characterization does not subject them to public control. Nor does the fact that they are affected with a public interest, because engaged in charitable work for the public's benefit, make them public corporations; it merely means they are operated for the public, generally, without profit. A hospital having the right, as does defendant hospital, to manage its own operations is a prviate hospital.

The new by-laws divided the hospital staff into several classes. Plaintiff contended that, because of his previous training, he should have received a higher classification and not been limited as to surgery he was allowed to perform. Plaintiff's contention, said the Court, amounted to a claim that he had a vested right to practice in the hospital. A doctor has no vested or constitutional right to practice in a private hospital, but merely a privilege which can be granted or denied even though his qualifications are of the highest and the hospital is not required to give any reason for excluding any doctor from its staff.

▶Can the doctrine of res ipsa loquitur be applied in a case involving paralysis following the administration of spinal anesthesia during childbirth?◀

The California Supreme Court had this question before it in *Seneris* vs *Haas*, 291 P. (2d) 915 (1955). Prior to delivery, plaintiff was given spinal anesthesia. When she awoke the next morning, she could not move her legs and had pains in her back, neck, head, arms and wrist. She regained the use of her right leg within three months but at the time of the trial she still suffered pain in her left hip and had only limited use of her left leg.

There was evidence that plaintiff had previously undergone spinal anesthesia with no ill effects. Plaintiff argued it was a matter of common knowledge that a woman does not ordinarily become permanently paralyzed following childbirth in which a spinal was used. The obstetrician testified that permanent paralysis does not ordinarly occur where proper care is used. The anesthetist's testimony was that in 4000-5000 spinals he had never had a resultant case of permanent paralysis and that paralysis could occur in spinal anesthesia even though there was no negligence.

Plaintiff contended the doctrine of res ipsa loquitur was applicable. The Court said that the conditions necessary for the doctrine's application are: (1) the injury must be of a kind not ordinarily occurring in the absence of someone's negligence; (2) it must be caused by an agency or instrumentality in defendant's control; and (3) it must not have been due to any voluntary action or contribution on plaintiff's part. The doctrine applies if, in the light of common experience, it can be said that defendant's negligence more likely than not caused the accident; it does not apply if no such balance of probabilities in favor of negligence can be found. Courts have relied on both common knowledge and expert testimony in determining whether such probability exists with respect to a particular occurrence. It appeared, said the Court, that plaintiff had made out a prima facie case, by both medical evidence and common knowledge, that her in-

juries were such as do not ordinarily occur in the absence of negligence; the anesthetist's evidence to the contrary raises an issue for the jury.

The anesthetist argued that plaintiff had failed to meet the doctrine's requirement that the injury must not have been due to any voluntary action or contribution by her. The basis of his argument was medical testimony that plaintiff suffered from a "psychic overlay factor" and the possibility she may have had a "sensitivity" to the anesthetic from which the paralysis developed. To rebut this argument, plaintiff produced evidence that she was, when admitted to the hospital, a strong, healthy woman suffering from no disease in which spinal anesthesia was contra-indicated and that she was presumptively non-allergic to spinal anesthesia because of a previous uneventful spinal anesthetic. The Court said that whether the conditions exists for the doctrine's application is a question of fact for the jury; plaintiff's evidence was sufficient to raise a question for the jury of whether the doctrine was applicable.

►Is it negligence to fail to inform a patient, prior to a blood transfusion, that he might contract viral hepatitis as a result thereof?◄

This question was decided by a Delaware Superior Court in *Fischer* vs *Wilmington General Hospital,* 149 A. (2d) 749 (1959). In the course of a dilation and curettement on the patient, who had suffered an incomplete abortion, she was given a transfusion of 500 cc's of whole blood. A short time later she was hospitalized for viral hepatitis, allegedly caused by the blood transfused. It is undisputed that the patient was not informed of the risk incident to the transfusion although it would have been possible to do so. The doctor who ordered the transfusion testified the patient's vaginal bleeding had been substantial and that, since the prime cause of maternal mortality is hemorrhages and resulting shock as compared with a fatality rate of less than .5% from hepatitis, it would have been negligent not to have given the transfusion because of the insignificant risk of communicating viral hepatitis. Another doctor stated it was the accepted practice in the community, in cases such as this, to give a transfusion, despite the risk of viral hepatitis. A doctor testifying for plaintiff stated that there are serious risks, other than viral hepatitis, attendant to a blood transfusion and that transfusions should not be given unless in the exercise of reasonable judgment they are necessary. Another doctor testified it was not in accordance with the practice of the profession in the community to advise patients of the risk that viral hepatitis may result from a transfusion, because the psychological and psychosomatic effect of the alarm produced by such advice would run counter to the beneficial effect sought to be produced by the transfusion itself. The Court said that, on the basis of the evidence, there was no legal duty to warn the patient that hepatitis might be communicated by the transfusion and there was, therefore, no negligence.

►When are medical treatises admissible in evidence over objection? If medical treatises are admitted in evidence by consent of the parties, what weight are they to be given?◄

These questions were before the Supreme Judicial Court of Maine in

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1958 in a workmen's compensation case, *Goldthwaite* vs *Sheraton Restaurant*, 145 A. (2d) 362. The plaintiff showed only slight immediate effects from a fall down the cellar stairs at her place of employment. A few days later, when she experienced pain in her lower back, she consulted a doctor. Her condition steadily deteriorated and three months after the fall she had to stop work altogether. It has now been determined that she is suffering from progressive muscular atrophy.

Plaintiff's doctor testified that, in his opinion, her disability could have been caused by the fall. An expert witness for defendant testified, on direct examination, that trauma could never cause or accelerate progressive muscular atrophy; as authority for his statement he cited a textbook of neurology, Kinnier Wilson. By agreement of the parties, abstracts from various medical textbooks and authorities were submitted in evidence. None of these authorities ruled out trauma as a precipitating or accelerating cause of muscular atrophy; several of them, including Kinnier Wilson, recognized trauma as a probable precipitating or accelerating cause. In deciding plaintiff's disability was compensable, the commissioner gave weight to: (1) her excellent health prior to the fall; (2) the rapid onset of symptoms of muscular atrophy after the fall and the steady deterioration of her condition thereafter; (3) her doctor's medical opinion; and (4) the abstracts from medical authorities supporting her doctor's opinion and contradicting that of defendant's expert witness.

Defendant contended there was no legally competent evidence to support the decision because the opinion of plaintiff's doctor was at best conjectural and the medical treatises were hearsay evidence. The Court said the severity of the fall and the marked change in plaintiff's health shortly thereafter were some evidence of the accidental cause of the disability. Her doctor's opinion, even though disputed by other medical experts, was competent legal evidence to be considered by the commissioner. Turning to a consideration of the abstracts from the medical treatises, the Court stated that the rule is that medical treatises are not admissible to prove the truth of the statements they contain; their admission would violate the rule against hearsay evidence. However, they are admissible, over objection, when offered to impeach a medical witness who relies at least in part upon medical authority for the opinion he has expressed. On direct examination, defendant's medical witness cited Kinnier Wilson as a recognized authority supporting his opinion. Plaintiff could then have used recognized authorities for the limited purpose of impeaching the witness. Defendent argued that the commissioner failed to limit his use of the evidence to impeachment but rather gave weight to it as evidence of the truth of the matter asserted. The Court said the evidence was properly received, although hearsay, because the parties agreed to its admission and the agreement did not limit its use. Such evidence is to be given its natural and logical probative effect. However, the fact-finder must keep in mind the inherent weakness which, if the evidence had been objected to, would have led to its exclusion. Such "consent evidence" may be given weight as corroborative of other competent legal evidence but will

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References: Rosenblum, L. A.: Clin. Med. 6:72, Jan. 1959.

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not alone support a finding. Written hearsay is more trustworthy than oral hearsay. A fortiori, when dealing with the writings of a recognized medical authority who has no motive for falsification, who is bound by the ethics of his profession and who is writing for the critical eye of others in the profession, his writings will often have very real and practical evidentiary value. The weakness of such evidence is that the author is not present in Court to be cross-examined and it cannot be known with certainty that his opinion is the same now as it was when he wrote the treatise. The Court said although the medical abstracts retained their hearsay characteristics, the commissioner did not err in giving them corroborative weight. They supported the opinion of plaintiff's doctor which, together with other competent evidence, justified a finding that trauma accelerated the muscular atrophy.◄

Reduction of High Serum Cholesterol

It has been suggested that the state of cholesterol in the serum rather than the quantity could be an important factor in atherogenesis. While the mode of action of the polysorbate 80-choline-inositol complex is as yet unknown, it was recently reported that the complex stabilizes the "abnormal" cholesterol present in essential hypercholesteremia. Polysorbate 80 is a complex mixture resulting from the reaction of ethylene oxide with a sorbitan fatty acid ester that has the ability to render fats and fat-soluble substances dispersible in aqueous media.

Polysorbate 80 was administered to a group of more than 100 subjects for periods up to four years in amounts of 4.5 to 6.0 gm. daily. No deleterious effects were noted in any patient. Since the agent was administered as an aid in the absorption of fat, it was of interest that the blood cholesterol levels were not raised.

Forty-one patients with hypercholesteremia associated with various pathological entities were treated with a polysorbate 80-choline-inositol complex. In each instance rigid dietary restrictions had failed to induce significant reduction of serum cholesterol levels. The cases of exogenous obesity had already been placed on a low-calorie, low-fat diet, without adjunctive therapy. The patients with peripheral vascular disease were on low-cholesterol diets plus peripheral vasodilator drugs; two of these had undergone sympathectomy and one an amputation. The mixture was given in doses of 10 cc. twice daily, in some cases increased to 40 to 60 cc. in 24 hours. In all patients there was a significant fall in serum cholesterol; in general, the higher the initial level, the greater the reduction achieved. Normal cholesterol levels were maintained only upon uninterrupted therapy. A sense of well-being was described by many of the patients, but a functional basis for this could not be excluded. No significant side effects were encountered

The long range effect of reducing hypercholestermic levels, particularly with respect to the possibility of reducing arterial disease, remains to be established.

Fuller, H. L., *Maryland M.J.*, 8:6-13,1959.

The Doctor Builds His Estate

Prepared for the readers of Clinical Medicine by the Research Department of the leading investment banking and brokerage firm of Bache & Co., 36 Wall Street, New York 5, New York

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These monthly articles point out one method by which the professional man may overcome the particular handicap imposed upon him by our tax structure, which taxes the bulk of his income at normal income tax rates, as opposed to the capital gains tax avenue open to many business men. One solution to this problem is the systematic investment of a portion of current income each year in securities. Such a program, which should include many different types of investments such as bonds, preferred stock, common shares and shares of mutual funds, will have as its objectives growth of principal together with reasonable income. We again emphasize that even the most complete series of articles of this type cannot take the place of consultation with a representative of a reputable brokerage firm.

Get any group of experienced investors or financial people together, listen to their talk about stocks, and one word you'll hear time and again will be "multiples." Investors for generations have found multiples, the price-earnings ratio of common stocks, to be handy rules of thumb in judging values. Over the years, moreover, the worth of this rule has been proven by the fact that stocks which sell at a certain multiple for a period of years frequently tend to sell at similar multiples in the future.

Thus, the analyst or investor able to forecast earnings of a firm with any degree of accuracy may have some idea of the price the market will be willing to pay for the stock

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when the earnings are achieved.

Of course, this is a gross oversimplification of the many problems of security analysis. For one thing, multiples occasionally change—the price-earnings ratios investors are willing to pay for chemical and aluminum companies have risen sharply in the past five years. Then too, many other factors beside multiples play a part in the price of a stock—dividends, industry outlook, market psychology at the moment, etc.

With this caveat in mind, this month we are discussing three stocks selling at multiples which are low either in relation to their competitors and/or in relation to historical precedent. In addition, earnings of all three are rising and the outlook is encouraging, leading up to anticipated continued earnings improvement.

The issues are P. Lorillard, fourth ranking cigarette producer in the United States; Smith-Douglass Chemical, an important producer of agricultural chemicals; and Walter E. Heller, one of the nation's leading factors.

P. LORILLARD COMPANY

P. Lorillard's common shares, selling at only 11 times 1958 earnings with an indicated yield of 5.2% still appear an attractive purchase for the investor seeking income with the possibility of capital appreciation. The company has dramatically improved its position in the industry in the past two years and we look for continued, if less spectacular gains in the future. Despite cancer scares which from time to time have had a temporary effect on the tobacco equities, more people continue to smoke cigarettes.

In terms of total sales, Lorillard ranks fourth, trailing R. J. Reynolds, American Tobacco and Liggett & Myers in that order. It has been estimated that Lorillard's volume today accounts for roughly 12% of total U.S. cigarette output as compared with roughly 6½% just five years ago. Sales of cigarettes account for 95% of LL's gross, principally for domestic consumption. Their main brands include Kent, Newport, Old Gold Filters and Old Gold Straights. Lorillard also manufactures Embassy and various turkish cigarettes, although sales of these products are minor. The remainder of their volume is comprised of sales of smoking tobacco, chewing tobacco and a brand of little cigars called Between The Acts.

Lorillard is more heavily dependent on the filter-tip market than its competitors—about 85% of their domestic sales are in that market compared with 45.9% for the industry as a whole. As a result, the company has benefited most from the nationwide expansion in the demand for filters which continued to increase during the past year. Filter sales accounted for 45.9% of the total domestic market in 1958 as opposed to 39.9% in 1957 and only 10% some five years ago. Trade sources estimate that filters will account for half of industry sales in 1959.

Over the past ten years, Lorillard's sales and per-share earnings have increased by 226% with the bulk of the gain coming in the past two years. The striking increase in sales and net in 1958 was due to the strong acceptance of Kent, which showed a unit sales rise of 138% over 1957. Prior to the introduction of Kent, Lorillard had lagged behind the rest of the industry in terms of profitability and sales and earnings advances.

Newport, Lorillard's mentholated

filter tip introduced late in 1957, showed a 1958 unit sales gain of 188% and is now on its way to becoming a major brand, although menthol cigarettes account for only 10.5% of the tobacco industry unit sales. Newport ranks third in this category behind Salem and Kools.

As a result of strength in the sales of both Kent and Newport, earnings jumped to a new high of $4.01 per share in 1958, up from $1.64, while sales rose 61%. The tobacco industry is a very competitve field in which advertising and promotion are keys to success. Leaf tobacco and advertising costs, the two principal cost factors, have increased over the years. To offset these rising expenses the cigarette companies use less and lower grade tobacco as well as reconstituted leaf tobacco. Thus, industry margins have increased in spite of rising costs. The firm was able to bring up its profit margins to a level commensurate with the industry leaders and the return on equity and capital were sharply improved.

First quarter 1959 sales were 9.4% ahead of the same period last year. Lorillard reports that sales of Kent and Newport have been increasing each month while sales of Old Gold Straights and Old Gold Filters have begun to level off after a decline last year. We look for sales for the full year to run well ahead of 1958 and estimate that earnings should range between $4.30 and $4.60 for the year, up moderately from 1958's $4.01. Net income was up 11% for the first quarter of 1959 and reported per-share earnings were 91¢ compared with 85¢ in the same period last year. These figures are adjusted to reflect both the increase in the number of outstanding shares as a result of a financing late in 1958 and a subsequent 2-for-1 split. Proceeds from the sale of 364,620 shares were used to reduce short term bank loans, which fluctuate from time to time depending on the volume of sales and tobacco purchases. This financing was necessary as a result of expanding volume of business, and after the stock issue the company's current financial condition was adequate and there was $50.75 million of long-term debt outstanding. We expect that the firm will continue dividends at 50¢ quarterly plus a year-end extra of 47½¢ in line with the 95¢ extra paid last year on the unsplit stock.

A change in the Government's method of collecting taxes that just became effective should eliminate the tobacco companies' need for tying up large sums of money in working capital for the purchase of tax stamps. It is no longer necessary for Treasury tax stamps to be on the package and the companies may now pay tax after their products are sold, on a bi-weekly basis, rather than before the sale on a daily basis as heretofore. Thus, the substantial amount of short term funds used to finance these tax stamps should be reduced.

The company's research department has been working on a new low-tar and low-nicotine cigarette, a factor which contributed to recent strength in the shares. At the present time, we do not know when this product will be released or its possibilities of success. Nevertheless, we feel that Lorillard is likely to pace the cigarette industry in its future growth and that its research department will continue to contribute the new developments essential to the maintenance of a strong competitive position.

P. LORILLARD & COMPANY

		Capitalization (12/31/58)	
Price	48	Long-term debt	$50,750,000
Dividend	$2.47½	7% Cum. Pref.	
Yield	5.2%	($100 par value)	98,000 shs.
1959 Price Range	48⅝-37	Common stock (10 par)	3,282,024 shs.
Traded	N.Y.S.E.		

SMITH-DOUGLASS COMPANY, INC.

Smith-Douglass, an important Southern and Mid-Western producer of fertilizers and animal feed supplements, is currently enjoying the fruits of a heavy investment program which at long last is being reflected in sharply improved earning power. For the fiscal year ended July 31, 1959, we estimate earnings of $2.60-$2.75 per share and sales of approximately $45 million compared with income of $1.46 per share on sales of $39.9 million in the previous fiscal year. Weather and political conditions permitting, further satisfactory gains are anticipated for the 1960 fiscal year.

There are two major explanations for Smith-Douglass' dramatic operating improvement. First, almost all producers of fertilizers now are experiencing substantially improved demand over the last year because of relatively more favorable weather conditions and higher farm income. Moreover, farm chemical makers are benefiting from a change in the Government's farm program which this year restored certain acreage to planting, particularly in the corn and cotton growing areas. For these reasons, mainly, trade sources expect a 20% gain in fertilizer consumption in the South and about 8% in the Midwest, both prime Smith-Douglass market areas.

The second explanation for the company's improvement can be traced to internal rather than general external factors. In May of 1957, Smith-Douglass acquired for $500,000 the stock of Texas City Chemical which has constructed $6 million in fertilizer and feed supplement facilities but was unable to operate profitably largely because of a heavy debt burden. Following a Federal court reorganization which involved a reduction of the debt structure, Smith-Douglass took over the defunct company and commenced a capital improvement program designed to restore Texas City to a profitable basis. This program, of course, required time and money and in its 1958 fiscal year, Smith-Douglass incurred a loss of 43¢ per share on its new operation. By June 1958, shortly before the end of the 1958 fiscal year, Texas City reached a break-even point and since then has become profitable. This turnabout, therefore, accounts for an important measure of this year's improvement with the likelihood of more to come in 1960.

A third element of future interest in the company's recent announcement of its intention to acquire Smith Agricultural Chemical in exchange for Smith-Douglass straight and convertible preferred stock at an effective price of about $1.9 million. Smith Agricultural has a book value of over $3.2 million and sales in excess of $10 million. The acquisition will strengthen Smith-Douglass' position in Ohio, Indiana and Michigan where the parent company presently is not

SMITH-DOUGLASS COMPANY, INC.

Price	27
Dividend	$1.20
Yield	4.4%
1959 Price Range	29⅜-22⅞
Traded	N.Y.S.E.

Capitalization (7/31/58)

Long-term debt	$8,824,771
$5 Cum. ($100 Par Pfd.)	28,420 shs.
Common stock ($1 Par)	944,288 shs.

efficiently represented. Smith, which used to earn $300-$500,000 per year in the early 1950s, has not lately been more than modestly profitable. Depreciation and other non-cash charges, however, have been throwing off about $240,000 per year, an important element in evaluation. Under the guidance of more aggressive Smith-Douglass merchandising techniques, the new company could develop into still another respectable source of new profits by 1960 and 1961.

Smith-Douglass' financial condition is quite satisfactory especially since the company's debt structure was recast in 1958 permitting a considerably easier sinking fund schedule on its debt. Furthermore, depreciation in 1958 was $1.88 per share indicating 1959 cash earnings of over $4.50 per share. Considering that capital expenditures are now expected to taper off, an increase in the five-year old $1.20 annual dividend rate seems both reasonable and likely.

In our opinion, the investing public will pay increasing attention to internal Smith-Douglass operating improvements. The shares, while somewhat speculative because of the vagaries of the weather and politics, appear relatively undervalued at 10 times 1959 earnings and 6 times cash flow. We recommend purchase, therefore, for income and capital gains in this reasonably valued equity, something of a rarity in today's enthusiastic stock market.

WALTER E. HELLER & COMPANY

The shares of W. E. Heller at current levels are not yet reflecting the sharp increase in earning power now underway and the excellent past record. Earnings for this year are estimated in the $2.75-$3.00 a share range and a further increase is projected for next year. Furthermore, as earnings projections are realized, an increase in the dividend is a distinct possibility. We would recommend these shares for investors interested in capital gains possibilities and long-term growth.

The principal activities of the company may be divided into the following seven main categories:

1. *Rediscounts:* The company purchases rediscounts or makes advances on loans against other finance company paper. Collections are usually made by the finance companies from which the paper is acquired, such companies also guaranteeing to pay, repurchase or replace defaulted paper.

2. *Commercial Installment Notes Receivable:* Installment notes payable in monthly installments ranging from a few months to 24 months or more are purchased from various business concerns. Such paper is usually secured by a lien on various articles, the normal life of which exceeds the term of the paper and by a guaranty of payment by the assignor, although some paper is purchased without a guaranty.

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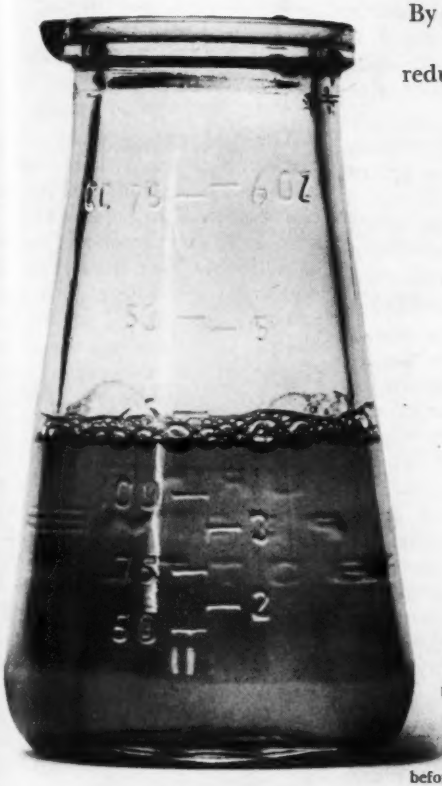

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3. *Commercial Accounts Receivable:* The company purchases or makes loans against the sales accounts of clients.

4. *Commercial Loans on Collateral:* The company also makes loans on plant, machinery, equipment and other chattels. Usually such loans are secured by chattel mortgages and the property is protected by insurance.

5. *Factored Accounts Receivable:* The company has been engaged in factoring the sales of wholesalers, manufacturers, mills or other concerns.

6. *Inventory Loans:* In conjunction with the purchase or advances against or factoring of accounts receivable, it sometimes makes loans on inventory. Usually the advance ranges from 50% to 80% of the customer's cost.

7. *Motion Picture & Television Production Loans:* The company makes loans secured by a first lien on the assets of the production, consisting of copyrights, the film itself, literary and musical material and 16 mm rights and television rights, as well as the income derived from exhibition. The company has also made loans on a first lien basis on several series of films designed for exhibition on television. To the extent that such loans are covered by film rental contracts for fully completed series, they are transferred to commercial installments notes receivable.

Gross receivables in 1958, which was not particularly a good year, rose to $191.6 million, a gain of 5.7% over the $180.9 million on the books in 1958. In May of this year, however, gross receivables jumped sharply to $213.7 million, up $22.1 million from year-end and up $35.7 million from May 1958.

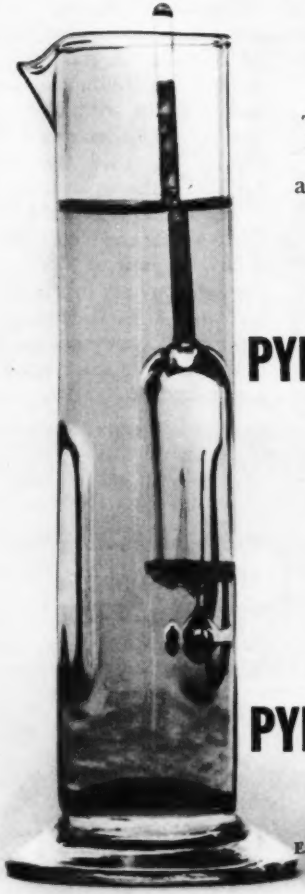
The current strong demand for additional working capital requirements by American industry is, of course, being reflected in the operations of the company and will continue to be reflected as the boom continues and money becomes tighter. Tight money not only increases the company's volume but exposes many firms in diversified industries to Heller's services. Experience has been that the new customer tends to stay with Heller even after money gets easier. Of course, it is this factor that is the most important in a long-term evaluation of the company's prospects.

The financial services offered by Heller for the most part complement financial services offered by commercial banks. Thus, competitive pressure on interest rates and volume are lessened. In fact, many of Heller's customers are referred to the company by commercial banks. Looking ahead, it is our opinion that the growth rate of the past decade will continue. Furthermore, Heller has shown the ability to maintain profit margins on higher volume.

Earnings for the 6 months ending June 30th should be about $1.30 a share compared with $1.18 a share in the similar period of 1958. For the first quarter, earnings were 56¢ a share, unchanged from the year earlier figures. In the first quarter, the comparison reflected the additional 125,000 shares sold in April 1958. Comparisons from now till the end of the year should be more favorable since the dilution will be fully reflected in the year-earlier figures.

For the full year we are estimating earnings of between $2.75-$3.00 compared with $2.39 last year and $2.24 in 1957. Furthermore, based on the current record volume of receivables and unearned discount on the books,

controls acute urinary tract infection and pain



It takes two therapies to assure fullest symptomatic and infection control, and Pyridium Tri-Sulfa provides them both in one ℞ for your convenience. The Pyridium component allays the pain, burning, urgency and frequency within 30 minutes ... while the classic triple-sulfa provides prompt therapeutic blood levels, often with the first dose, to control the infection.

PYRIDIUM TRI-SULFA

PYRIDIUM® TRI-SULFA

phenylazo-trisulfapyrimidine

DOSAGE: *Adults*—first day, 2 tablets four times daily. Then 1 tablet four times daily.

SUPPLIED: Bottles of 30 tablets.
Each tablet contains: Pyridium® (Brand of phenylazo-diamino-pyridine HCl) ... 150.0 mg.;
Sulfadiazine ... 167.0 mg.;
Sulfamerazine ... 167.0 mg.;
Sulfamethazine ... 167.0 mg.

WARNER CHILCOTT
MORRIS PLAINS, N.J.

1 tab. q.i.d....rapid analgesia...high sulfa blood levels

WALTER E. HELLER & COMPANY

Price	28
Dividend	$1.20
Yield	4.28%
1959 Price Range	31⅛-27¼
Traded	N.Y.S.E.

Capitalization (3/31/59)	
Long-term debt	$55,793,333
Pfd. Stock ($100 Par)	60,568 shs.
Common stock	1,470,217 shs.

we believe that Heller in the next 12 months (July 1, 1959 to June 30, 1960) could show earnings of $3.25-$3.60 a share.

Capital funds as of year-end 1958 amounted to $28.7 million or $15.69 a share. Capital funds supported $58.4 million of subordinated and unsubordinated debt and $76.6 million of notes payable. Current maturities of long-term debt will be $2.1 million and in 1960 $1.4 million. Since the end of the year, the company sold $3 million of 5½% subordinated notes due 1974 and 1 million convertible (into 30,000 shares) 5% junior subordinated notes due 1974. Also, on March 3rd of this year, Heller acquired the Refinance Corporation of Los Angeles with assets of $2.0 million for 18,500 common shares. As of March 31, 1959 the company had 1,470,217 shares outstanding.

The current annual dividend rate is $1.20 a share, which represents about a 50% payout of 1958 earnings. The average payout in the last five years has been 47%. If earnings projections are realized, increases in the dividend both this year and next are a distinct possibility.◄

Tentone Tablets *(Lederle)*

Phenothiazine derivative. Each tablet contains *either* 10, 25 *or* 50 mg. of methoxypromazine maleate. *Indications:* For conditions requiring psychiatric assistance but where constant supervision is not necessary. Mild to moderate anxiety states, obsessive-compulsive behavior patterns, psychoneurotic affective disorders, anxiety following trauma, situational anxiety and hysteria, chronic anxiety, tension states secondary to the menopausal syndrome. *Dosage:* As directed by the physician. *Supplied:* Tablets of 10, 25 or 50 mg., in bottles containing 100 or 1000 tablets.

Polykol Capsules *(Upjohn)*

New dosage form. Each capsule contains 250 mg. of oxyethylene oxypropylene polymer. *Indications:* Oral wetting agent for the prevention and treatment of constipation associated with hard, dry stools. *Dosage:* Adults, 2 or 3 capsules daily until regularity is established, then 1 or 2 capsules daily as needed. Children, 6 to 12 years, 1 or 2 capsules daily until regularity is established. *Supplied:* In bottles containing 16 or 100 capsules.

Marax *(Roerig)*

Combination tablet containing 10 mg. hydroxyzine hydrochloride, 25 mg. ephedrine sulfate and 130 mg. theophylline. *Indications:* For control of bronchospastic disorders such as asthma, hay fever and allied allergic conditions. *Contraindications:* Cardiovascular disease, hyperthyroidism and hypertension. *Dosage:* According to severity of complaints and toleration. Usual dose for adults is 1 tablet 2 to 4 times daily. Children, half the usual adult dose. *Supplied:* In bottles containing 100 tablets.

Actase Fibrinolysin *(Human)* *(Ortho)*

A naturally derived fraction of human blood. *Indications:* For intravenous dissolution of blood clots in cases of pulmonary embolism and thrombophlebitis. *Contraindications:* Any hemorrhagic diathesis, major liver dysfunction, hypofibrinogenemia. *Dosage:* For intravenous infusion as directed by the physician. *Supplied:* In vials containing 50,000 fibrinolytic units, to be stored at 0° to 10° C.

Neo-Aristocort Eye-Ear Ointment 0.1% *(Lederle)*

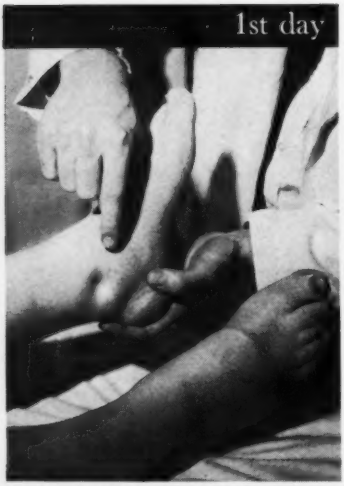
Each gram contains 1 mg. *Aristocort* (triamcinolone acetonide) and 5 mg. neomycin sulfate (equivalent to 3.5 mg. of neomycin base). *Indications:* As a counteracting influence on the cause of inflammation and fever found in many ocular infections, allergic reactions, traumatic and postoperative conditions. *Dosage:* As directed by the physician. *Supplied:* In tubes containing ⅛ ounce of ointment.

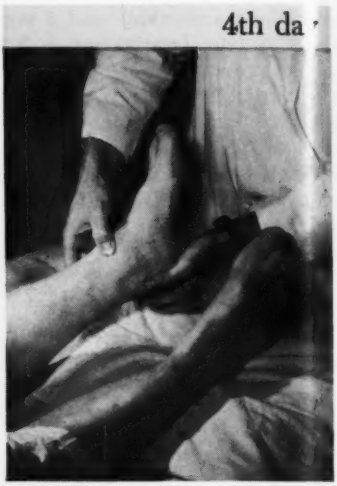
Betadine Vaginal Gel *(Tailby-Nason)*

Contains povidone-iodine as active ingredient. *Indications:* In the treatment of vaginal moniliasis, trichomoniasis and nonspecific vaginitis. *Dosage:* One applicatorful of gel inserted each night, followed by a douche the next morning through the entire menstrual cycle. If further therapy is warranted, the gel should be continued only during the actual menses days of the following two menstrual periods. *Supplied:* In 3 ounce tubes with applicator.

Meti-Derm Aerosol and Meti-Derm with Neomycin Aerosol *(Schering)*

New size. Pocket sized 50 gm. containers to provide patients with a convenient means of treating inflammatory dermatoses on the job. *Indications:* For topical treatment of inflammatory dermatoses, or dermatoses complicated or threatened by secondary infection. *Dosage:* Apply topically as directed by the physician. *Supplied:* In 50 gm. aerosol containers.





Record of patient with congestive failure, treated at a leading Philadelphia hospital. Photos used with permission of the patient.

marked pitting edema (4+) cleared in 4 days with Esidrix

Highest fluid yields, lowest blood-pressure levels yet achieved with oral diuretic-antihypertensive therapy.

Esidrix, 10 to 15 times more active than chlorothiazide, is indicated in... congestive heart failure • hypertension • hypertensive vascular disease • premenstrual edema • toxemia of pregnancy • edema of pregnancy • steroid-induced edema • nephrosis • nephritis

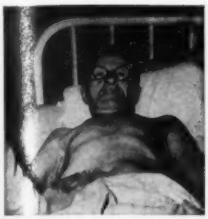
DOSAGE: Esidrix is administered orally in an average dose of 75 to 100 mg. daily, with a range of 25 to 200 mg. A single dose may be given in the morning or tablets may be administered 2 or 3 times a day.

SUPPLIED: *Tablets*, 25 mg. (pink, scored); bottles of 100 and 1000. *Tablets*, 50 mg. (yellow, scored); bottles of 100 and 1000.

C I B A SUMMIT, N.J.

2/2108MX

remember **Serpasil®** (reserpine CIBA) for the anxious hypertensive with or without tachycardia



L.S. 81 years – presenting complaint, painless hematuria 3/3/59. **Symptoms:** expiratory wheezes over entire chest; bilateral coarse rales of both bases; slight abdominal distention; palpable liver 2-3 fingerbreadths below rib cage; bilateral pitting edema (4+) of pretibial and ankle areas. **Diagnosis:** hematuria; arteriosclerotic cardiovascular disease; poorly compensated heart failure; and chronic pulmonary fibrosis with pulmonary insufficiency.

Patient was put on regimen of bed rest, moderate salt restriction, digitalis and pulmonary decongestants. When ankle edema, hepatic congestion and rales failed to clear by 3/6, Esidrix 50 mg. b.i.d. was ordered. By 3/8 L.S. had lost 3 pounds. Rales decreased; there was 1+ pitting edema of ankle area only. He felt more comfortable, was able to enjoy reading newspapers and magazines in bed.

Ambulatory on the 4th day of Esidrix therapy, L.S. visited his neighbors down the hall, played checkers with another patient. There was no evidence of ankle edema. By 3/11, patient's weight had dropped 2 more pounds and rales were gone. Patient tolerated cystoscopy and fulguration of a small bleeding polyp in his bladder on 3/12 very well. On 3/14 he was discharged.

Record of patient with congestive failure, treated at a leading Philadelphia hospital. Photos used with permission of the patient.

Patient L.S. Date	3/4	3/5	3/6	3/7	3/8	3/9	3/10	3/11	3/12	3/13
Urinary Output (ml.)	840	690	960	2140	1230	660	1220	1350	—	—
Weight (lbs.)	139	—	—	—	136	—	—	134	—	—
Esidrix Dosage (mg./day)	0	0	50	100	100	100	100	100	50	100

Esidrix T.M.

(hydrochlorothiazide CIBA)

- **relieves edema in many patients refractory to other diuretics[1]**
- **often produces greater weight loss than parenteral mercurials or chlorothiazide[2]**
- **provides a greater average reduction in blood pressure than chlorothiazide[3]**
- **is exceptionally safe . . . reduces the likelihood of electrolyte imbalance**

1. Brest, A. N., and Likoff, W.: Am. J. Cardiol. 3:144 (Feb.) 1959. 2. Clark, G. M.: Clinical report to CIBA. 3. Dennis, E. W.: Clinical report to CIBA.

Tepanil *(National Drug)*

Anorexic. Each tablet contains 25 mg. diethylpropion. *Indications:* For use in weight reduction. *Dosage:* One tablet 3 times daily, ½ hour before meals. An additional tablet may be given in the evening. *Supplied:* In bottles containing 100 tablets.

S.A. Vite *(Ayerst)*

Sustained action (controlled release) therapeutic multivitamin tablet. *Indications:* For multivitamin support wherever nutritional therapy is indicated. *Dosage:* One tablet daily, preferably at breakfast. *Supplied:* In bottles containing 60 or 500 tablets.

Ger-O-Foam *(Geriatric Pharm.)*

Aerosol anesthetic, analgesic foam. Methyl salicylate, benzocaine, volatile oils in an emulsion base. *Indications:* Musculoskeletal disorders such as rheumatoid arthritis, osteoarthritis, painful limbs following C.V.A., rotator-cuff tendinitis, painful healed fracture, fibromyositis, torn muscle, phantom limb pain, muscle sprains and low back pain. *Dosage:* Apply topically and gently massage affected area. *Supplied:* In aerosol cans.

Pentothal Sodium Rectal Suspension *(Abbott)*

New product form. Each gram of suspension contains 400 mg. of thiopental sodium with 24 mg. anhydrous sodium carbonate as a buffer, in a water-miscible mineral oil suspension. *Indications:* Whenever preanesthetic sedation or basal narcosis by the rectal route is desired. *Dosage:* Average dose for hypnosis is 1 gm. per 75 pounds of body weight. When a more profound response (basal narcosis) is desired, dosage may be increased to 1 gm. per 50 pounds of body weight if the patient is normally active and robust. *Supplied:* In *Abbo-Sert* package containing 5 gm. of suspension.

Anturan *(Geigy)*

Each tablet contains 100 mg. sulfinpyrazone. *Indications:* For use in the long-range management of chronic gout. *Dosage:* As directed by the physician. *Supplied:* In bottles containing 100 tablets.

BOOK REVIEWS

Playing for Life, Billy Talbert's Story

by William F. Talbert with John Sharnik. With photographs. Little, Brown and Company, Boston. 1958, 1959. $4.00

Very few autobiographies make attractive reading. This partial biography has the advantage over most of being written by a man who has been well instructed in the use of language and of good manners. Evidences of these two qualities make the book worth reading, especially by the minority who do not believe that play is the end and purpose of existence.

A Handbook of Obstetrics & Gynecology for Nurses

by Douglas G. Wilson Clyne, B.M., B. Ch., M.A. (Oxon.), L.R.C.P., F.R.C.S. (Edin.), M.R.C.O.G., Barrister-at-law, Examiner to the Central Midwives Board and to the General Nursing Council for England and Wales. Later Registrar and Tutor, Charing Cross Hospital, and Honorary Registrar to the General Lying-in Hospital. John Wright & Sons Ltd., Bristol. The Williams & Wilkins Company, Baltimore. 1958. $4.00

This reviewer has never thought well of the practice of beginning a medical or surgical textbook with copy from books of anatomy and physiology. There may be such need in a book for nurses. It may be taken for granted that any book put out by so eminent an authority in so many fields is well deserving of choice as a textbook. The parts of the book that deal with clinical matters will serve their purpose admirably.

Your Mind Can Make You Sick or Well

by Curt S. Wachtel, M.D., Prentice-Hall, Inc., Englewood Cliffs, N. J. 1959. $4.95

From almost the beginning of mankind it has been known that mind, or the lack of it, greatly influences matter. This is but recognition of the fact that the dog has a tail to wag. It is not, however, an admission that the tail had a dog to wag. This book is one of the many writings appearing lately that grossly exaggerate the influence of mind on health or illness. The author gives his name, but remains noncommittal as to what or who he is.

Now or Never, The Promise of the Middle Years

by Smiley Blanton, M.D., with Arthur Gordon. Prentice-Hall, Inc., New York, N.Y. 1959. $4.95

My own observation does not agree with that of so many who believe that the majority of those in middle life are unhappy. That minority of such persons who are unhappy, or even miserable, can find much to make their lives more endurable, perhaps even cheerful, by reading these pages—and not taking what is told too seriously.

Long-Term Illness: Management of the Chronically Ill Patient

edited by Michael G. Wohl, M.D., F.A.C.P. Former Clinical Professor of Medicine (Endocrinology), Philadelphia General Hospital and Temple University School of Medicine; with the collaboration of 79 Contributing Authorities. W. B. Saunders Company, Philadelphia. 1959. $17.00

Certainly a good book covering this subject has been needed for a long time. The good sense of the author is attested by his choosing the title *Long-Term Illness* because chronic illness tends to convey a sense of hopelessness. A doctor who thinks that way could not possibly put out a poor medical book. Of the two sections, the first deals with general principles of hospital and home care, rehabilitation, and nursing procedures—with not too much about psychologic problems—in the chronically ill. The second section deals with treatment of disease entities. Therapeutic procedures receive special emphasis, and are described in sufficient detail.

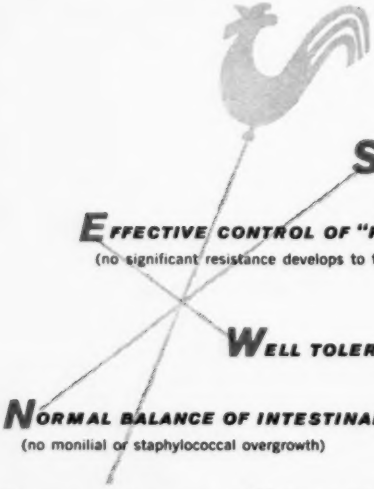
TO STOP DIARRHEA

from all points... growing evidence favors

FUROXONE®

brand of furazolidone

■ Pleasant-flavored LIQUID, 50 mg. per 15 cc. (with kaolin and pectin) ■ Convenient TABLETS, 100 mg. ■ Dosage—400 mg. daily for adults, 5 mg./Kg. daily for children (in 4 divided doses).



SWIFT RELIEF OF SYMPTOMS

EFFECTIVE CONTROL OF "PROBLEM" PATHOGENS
(no significant resistance develops to this wide-range bactericide)

WELL TOLERATED, VIRTUALLY NONTOXIC

NORMAL BALANCE OF INTESTINAL FLORA PRESERVED
(no monilial or staphylococcal overgrowth)

From a Large Midwestern University:

FUROXONE CONTROLS ANTIBIOTIC-RESISTANT OUTBREAK

An outbreak of bacillary dysentery due to Shigella sonnei was successfully controlled with FUROXONE after a broad-spectrum antibiotic had proved inadequate. Cure rates (verified by stool culture) were 87% with FUROXONE, 36% with chloramphenicol. Only FUROXONE "failures" were those lost to follow-up. Chloramphenicol failures subsequently treated with FUROXONE responded without exception. FUROXONE was also used effectively as prophylaxis and to eliminate the carrier state. It was "extremely well tolerated in all 191 individuals who received it either prophylactically or therapeutically." Galeota, W. R., and Moranville., B. A.: Student Medicine (in press)

EATON LABORATORIES, NORWICH, NEW YORK